Tuberculosis (TB)

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Tuberculosis (TB)

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TUBERCULOSIS MATRIX

Condition	Assessment		Education	Follow-up
Classification 0 No TB Exposure Not Infected	Patient TB Risk Assessment (TB-4) with targeting testing of persons in at-risk groups **Persons at Increased Risk for Mycobacterium tuberculosis Infection** • Close contacts of a person known or suspected to have active TB disease • Foreign-born persons, including children who have immigrated within the last 5 years from areas where TB is prevalent** • Persons who visits areas with a high TB prevalence, especially if visits are frequent or prolonged • Residents and employees of high-risk congregate settings • Health care workers (HCWs) who serve high-risk clients • Medically underserved, low income populations, homeless • High-risk racial or ethnic minority populations • Persons who abuse drugs or alcohol • Infants, children, and adolescents exposed to adults at high-risk for latent TB infection or active TB disease	Complete patient TB Risk Assessment (TB-4) prior to tuberculin skin test (TST) or blood assay for Mycobacterium tuberculosis (BAMT) for all classifications. TSTs are preferred for children aged less than five years. Tuberculin skin test (TST) with Purified Protein Derivative (PPD) using the **Mantoux method (use Tubersol antigen)** The TST must be given and read by a nurse per 902 KAR 20:016 A two-step TST is usually recommended initially for: • Anyone **required** to have **regular** TB testing, regardless of age BAMTs are one-step in-vitro tests that assess for the present of infection with *M. tuberculosis.*	Educate on signs and symptoms of active TB disease, risk factors for Latent TB Infection (LTBI), and risk factors for rapid progression from LTBI to active TB disease See procedure for TST in this reference. Review CDC TST Video, 2003 **Two-step TST:** • If first step TST is positive, consider the person infected. • If first step TST is negative, give the second step TST 1–3 weeks later. • If second step TST is positive, consider person infected. • If second step TST is negative, consider person uninfected. BAMT reported as positive, consider person infected. See TST Recommendations for Infants, Children, and Adolescents, p 14 in this reference	Some groups may need annual TB Risk Assessments (TB-4). Some groups, e.g. HCWs may need annual TSTs or BAMTs in addition to annual TB Risk Assessments (TB-4). All testing activities should be accompanied by a plan for follow-up care. Patients should return in 48–72 hours for TST reading, interpretation, and recording by nurse. Anergy Suspects Do not rule out TB diagnosis based on negative skin test result; consider anergy if immunosuppressed; also see other diseases/conditions that can cause suppression of delayed-type hypersensitivity (DTH) response. **Delayed type hypersensitivity (DTH) antigen tests are not recommended for administration at LHDs.**

* See *Core Curriculum on Tuberculosis* (2013) for TB Classification System. **See tables with international TB incidence and prevalence rates in this reference for more inform*ation.*

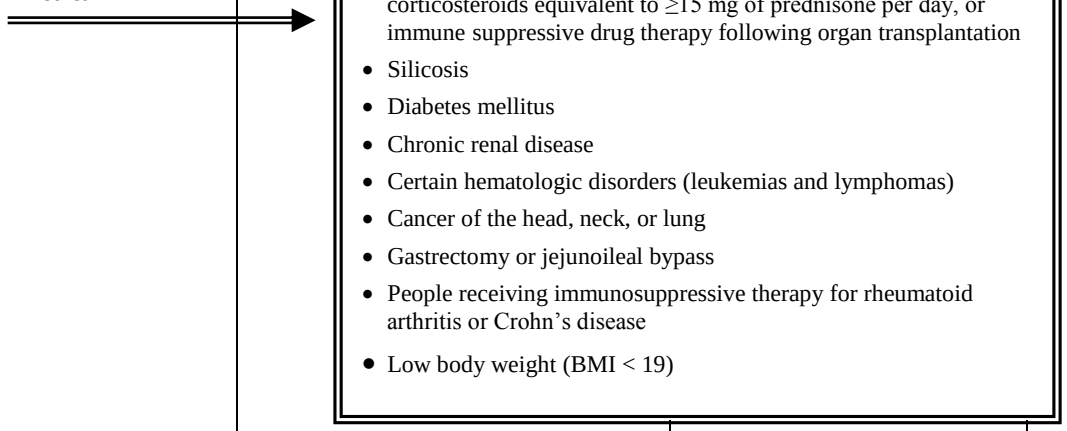
MMWR, Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection, June 9, 2000

1. Each LHD shall have a designated employee responsible for Tuberculosis (TB) services in their county. This person must attend periodic TB updates or keep updated by having the latest educational and scientific materials for the prevention and control of TB from CDC/ATS/ALA, the Southeastern National Tuberculosis Center, and other National Tuberculosis Centers.
2. The physician or clinician knowledgeable in the field of mycobacterial diseases shall provide patient care. They shall agree to update themselves through professional meetings, consultations, and review of journal articles. This must be a component of any LHD contract for TB clinician services.

This current classification system of tuberculosis (TB) is based on the pathogenesis of TB. A person with a classification of 3 or 5 should be receiving drug treatment for TB and should be reported to the LHD.*

TUBERCULOSIS MATRIX
(Continued)

Condition	Assessment		Education	Follow-up
Classification 0 (Continued) No TB Exposure Not Infected *Targeted Testing for low risk individuals is no longer recommended (2016 LTBI Guidelines; pg. e4)	Groups that **should** be TB Tested (Continued) **Persons at higher risk for developing active TB disease once infected** • Persons with HIV infection • Infants and children aged less than five (5) years • Persons recently infected with *Mycobacterium tuberculosis* (within the past two (2) years. • Cigarette smokers and persons who abuse drugs or alcohol • Persons with a history of inadequately treated TB • Persons with certain medical conditions	Develop a policy that the LHD will repeat TSTs given by other health care providers not trained by the LHD unless their skill is known and trusted by the LHD. LHDs DO NOT need a similar policy for repeating BAMTs. TSTs administered by LHDs can be read by staff in other LHDs and do not usually need to be repeated.		



TUBERCULOSIS MATRIX
(Continued)

Condition	Assessment	Treatment	Education	Follow-up
Classification 1 TB Exposure (contact), no evidence of infection	**Identify** contacts within **3 workdays** of suspect/case report, using prioritization and the Concentric Circle Approach (p. 41). Administer **TST or draw blood for BAMT and Examine** high-risk contacts within **7 workdays** of identification (See pages 37 and 46) Give TST or draw blood for BAMT for medium and low-risk contacts based on findings from the Concentric Circle Approach (See pages 41 and 46) Do the following: 1. Patient TB Risk Assessment (TB-4) 2. Medical History (TB H&P 13 or TB 20 follow up form) 3. TST or BAMT (unless there is previously documented positive reaction) 4. Chest x-ray, **at the same time** those who: • Have TB symptoms • Are HIV infected or have other immunosuppressed conditions • Are < 4 years of age Posterior–Anterior (PA) chest x-ray is the standard view used to detect abnormalities PA and lateral view should be done on those < 5 years of age If symptomatic, see sputum collection recommendations in this reference and in online forms.	Infants and Children <5 years of age, who are high priority contacts and who have a negative TST or negative BAMT, should be started on window period prophylaxis, with therapy administered by Directly Observed Preventive Therapy (DOPT) until retested in 8-10 weeks. If repeat TST or BAMT is positive, continue medicines by DOPT (see classification 2) If repeat TST or BAMT is negative, stop medicine unless contact with infectious case has not or cannot be broken. Contacts with immunocompromising conditions (e.g. HIV-infected) that have a negative TST or negative BAMT should be started on window prophylaxis therapy by DOPT until retested in 8-10 weeks. If the repeat TST or BAMT remains negative, and an evaluation for active TB disease is negative, a full course of treatment for LTBI should still be completed. See Medications to Treat LTBI in this reference	Discuss: • How TB is transmitted • LTBI versus active TB disease • Importance and significance of repeat skin test in 8-10 weeks • Treatment of active TB disease or LTBI • Importance of taking medicine on a regular basis if indicated Steps for patient producing a sputum specimen at home: • Clean & thoroughly rinse mouth with water • Breathe deeply 3 times (a tickling sensation at end of breath) • After 3rd breath, cough hard & try to bring up sputum from deep in lungs • Expectorate sputum into a sterile container collecting at least one teaspoonful • Perform this in a properly ventilated room, booth, or outdoors Provide patient information for an informed consent.	If TST or BAMT is negative, must return 8–10 weeks after contact has been broken, for repeat TST or BAMT. To avoid difficulty with test interpretation in a contact investigation, the follow-up TB test method for a particular contact, whether TST or BAMT, should preferably be the same test method used for the first TB test. Use of the same test method for repeat testing will minimize the number of conversions that occur because of test differences.

Self-Study Modules on Tuberculosis, Contact Investigation for Tuberculosis, CDC Core Curriculum on Tuberculosis (2013)
MMWR, Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection, June 9, 2000

TUBERCULOSIS MATRIX
(Continued)

Condition	Assessment	Treatment	Education	Follow-up
Classification 2 Infection **without** active TB disease • Positive TST (mm induration) or positive BAMT • Negative bacteriological studies (if done) • No clinical bacteriological or radiographic evidence of active TB disease.	Candidates for treatment of LTBI • See TST reaction classification or guidelines for BAMTs, this reference • **Careful assessment to rule out active TB disease is necessary before treatment for LTBI is started** • Immediately get a chest x-ray for patients **with symptoms** AND a positive TST or positive BAMT • Others should be given a chest x-ray as soon as possible. When TB disease is ruled out, treat for LTBI if indicated. • If chest x-ray abnormal, obtain sputum's, and consider as a suspect case • Determine history of prior treatment for LTBI or active TB disease • Determine if there are any medical conditions that are contraindications to treatment or would increase risk of adverse reactions • Provide HIV counseling, testing, and referral. If HIV test is refused, reoffer HIV testing monthly while on LTBI treatment. Baseline hepatic measurements recommended for: • Patients whose initial evaluation suggests a liver disorder or regular use of alcohol • Patient with HIV infection • Pregnant women and those in immediate post-partum period (3 months, especially Black and Hispanic women) • Patients with history of chronic liver disease (e.g., hepatitis B or hepatitis C)	See LTBI regimens in this reference The following groups are considered to be high-risk individuals when it comes to being adherent to taking their medications. If found to have LTBI, these groups must be placed on Directly Observed Preventive Therapy (DOPT): • Children and adolescents • Contacts to a case with active TB disease • Homeless individuals • Persons who abuse substances • Persons with a history of treatment non-adherence • Immunocompromised patients, especially HIV-infected For any other persons, DOPT should be used if LTBI treatment is ordered twice weekly (See pages 39 - 43). Call the Kentucky TB Program to discuss twice-weekly treatment of LTBI.	Establish rapport with patient and emphasize: • Benefits of treatment • Importance of adherence to treatment regimen • Possible adverse side effects of medicine(s) • When to stop medication and call the local health department (LHD) • HIV testing with pre- and post-test counseling Directly Observed Preventive Therapy (DOPT) for LTBI is recommended for any at risk adults who cannot or will not reliably self-administer drugs **ATTENTION:** Medical providers should consult pages 39-43 of this reference about medications to treat LTBI in children and adolescents, doses, and intervals for administration by DOPT, unless medically contraindicated. Call the KY TB Program to discuss treatment of LTBI in children and adolescents.	`

*Centers for Disease Control and Prevention, Core Curriculum on Tuberculosis (*2013)
Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection, MMWR, June 9, 2000

TUBERCULOSIS MATRIX
(Continued)

Condition	Assessment	Treatment	Education	Follow-up
Classification 3 **TB disease, clinically active** Tuberculosis Case Definition: Positive Lab Test *Mycobacterium tuberculosis* culture *M. tuberculosis* complex demonstrated in Nucleic Acid Amplification (NAA) test or PCR test -or- Clinical Case: • Positive TST or positive BAMT • Abnormal changing chest x-ray *or* clinical evidence of disease • Placed on 2 or more antitubercular antibiotic drugs • **Completed** diagnostic evaluation to include a patient TB risk assessment (TB-4)	See Contact Investigation and the Concentric Circle approach in this reference Should be seen by local health department (LHD) physician as soon as possible if LHD is supplying TB medications Case Management • Assignment of responsibility • Systematic regular review • Plans to address barriers to adherence • Provide HIV counseling, testing, and referral. If HIV test is refused, reoffer HIV testing monthly while on treatment for active TB disease. Adherence • Non adherence is a major problem in TB control • Use case management and directly observed therapy (DOT) to ensure patients complete treatment. If more than 3 doses are missed, contact KY DPH TB staff. • Initially order AST, ALT, Bilirubin, Alkaline phosphatase, serum creatinine, and platelets for adults. Visual acuity and color vision as baseline if on EMB, question vision status monthly • Obtain baseline weight and monitor weights monthly Determine the Patient's clinical condition: • Immediately if not hospitalized • Within 3 days of notification if hospitalized (best to visit in hospital) • Basic physical exam done within 7 days of notification	Basic Principles of Treatment: ***Kentucky endorses Regimen 1 initially (The 4 drug TB antibiotic therapy; pg. 19)*** • Provide safest, most effective therapy in **shortest** time • Multiple drugs to which the organisms are susceptible • **Never** add single drug to failing regimen • Ensure adherence to therapy • DOT is the standard of care for all cases of active TB disease Management of HIV related active TB disease is complex; care should be provided by a consultant expert in both HIV and TB Pregnant Women • 9 month regimen - RIF, INH, and EMB • SM is contraindicated • In HIV-positive pregnant women, consult an expert, (SNTC Hotline 1-800-4TB-INFO) Notify the State TB Program about the prescribed regimen. Infants Treat as soon as tuberculosis is suspected. See regimens in this reference for treatment of adults, children, and those with extrapulmonary tuberculosis Tuberculosis caused by Drug Resistant Organisms Treatment should be done by, or in close consultation, with an expert in the management of these difficult situations Vitamin B6 10–25mg for those with certain conditions (e.g. HIV infection)	Instruct patient about: • Active TB disease and how it is spread • Importance of taking medications on a regular basis • Medication side effects and instructions to immediately report adverse reactions • Proper times and way to collect/mail sputum specimens • The taking of other medications and the potential risks of drug interactions • Importance of good nutrition • Tobacco cessation and nicotine replacement therapy Confinement and/or restriction of activities must be addressed (TB Control Law, KRS 215.540) KRS 215.531 states drug susceptibility test on initial TB isolates from patient with active TB disease must be ordered by the physician Ensure that all initial positive TB cultures from **independent labs** have drug susceptibility studies ordered by private physicians	• Monitor for Adverse Reactions • See Recommendations for Sputum Collection • Chest x-rays **initially,** at 2 months after starting therapy, and at 0 to 60 days after completion of therapy. Clinical case**s also nee**d chest x-ray after 2 months of multiple drug therapy • All efforts to follow-up must be documented in the patient's chart • A home visit must be done • Consult with DPH if the patient's status changes while on treatment *See Kentucky TB Control Law KRS 215* Directly Observed Therapy (DOT) • Health Department health care worker must watch patient swallow each dose of medication • DOT shall be the Kentucky standard of care for all cases of active TB disease • DOT must be used with all intermittent regimens • DOT can lead to reductions in relapse and acquired drug resistance • Use DOT with other measures to promote adherence • Court ordered DOT may be necessary • See DOT in this reference • For Video DOT protocols, see page 19 TB isolate from all specimens with a positive TB culture shall be sent to the Kentucky Department of Laboratory Services (DLS) for drug susceptibility and genotyping tests. LHD TB staff shall contact hospital labs, independent labs, or national reference labs to coordinate shipment of TB isolate to DLS. 902 KAR 2:020 http://www.lrc.ky.gov/kar/902/002/020.htm

Centers for Disease Control and Prevention, Core Curriculum on Tuberculosis (2013)

TUBERCULOSIS MATRIX
(Continued)

Condition	Assessment	Treatment	Education	Follow-up
Classification 4	TB no longer clinically active		Teach patient signs and symptoms of possible recurrence of active TB disease	
Classification 5	TB suspected. Diagnosis pending. Should not have this classification for more than three (3) months Results of a positive Nucleic Acid Amplification (NAA) test, e.g. Gen-Probe, on a sputum sample can help determine active TB disease with *Mycobacterium tuberculosis* (MTB)	If NAA test on sputum is positive, treatment should begin with a 4-drug regimen until TB is ruled out	Teach patient signs and symptoms of possible recurrence of active TB disease.	As indicated

Centers for Disease Control and Prevention, Core Curriculum on Tuberculosis (2013)

Recommendations for Sputum Collection

Purpose	Frequency	Number of Specimens
Baseline for TB suspects	Initial	3 samples that are collected 8 – 24 hours apart. Recommend at least one sample collection be observed by health care worker. **Obtain sputum samples BEFORE initiating tuberculosis therapy.**
NAA testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities.*		
Monitoring for **smear** and culture conversion (AFB Smear positive Culture positive)	**Every 2 weeks** after 2 weeks of therapy have been completed, until 3 consecutive AFB smears are negative. After 2 months of uninterrupted therapy. ***Note:*** *3 negative smears are required per 902 KAR 20:200 and 902 KAR 20:016*	→ 1 sample – Recommend collection be observed by health care worker → 3 samples on consecutive days. Recommend collection be observed by health care worker If still positive, treatment regimen must be re-evaluated
Monitoring during treatment for **culture** conversion (AFB Smear negative Culture positive)	**Every 2 weeks** until 2 consecutive specimens are negative on culture.	3 samples on consecutive days. Recommend at least one be observed by health care worker • Patients who have positive cultures after 4 months of treatment should be treated as treatment failures (MMWR, June 20, 2003)
Monitoring after culture conversion to negative (or a clinical case)	**Monthly** until treatment is completed. Patient may not be able to produce sputum at this point	1 sample. Recommend collection be observed by health care worker Frequency of collections may be increased if there is a recurrence of symptoms or treatment interruption. Patients with MDR-TB or HIV infection and TB may require additional sputum testing to monitor their clinical course Send specimens to the state lab and instruct private hospitals and physicians to use the state lab
Obtain three (3) consecutive sputum samples for any patient who has evidence of worsening clinical signs / symptoms of active TB disease (i.e. new cough, hemoptysis, fever, sweats, or worsening chest x-ray findings)**		

Source: ***MMWR 2009; 58(01):7-10**
****SNTC Clinical Consultation – July 2010**

GeneXpert MTB/RIF Assay TESTING PROTOCOL

Intended Use

The GeneXpert MTB/RIF Assay is intended for use with **sputum** specimens from patients for whom there is **clinical suspicion of tuberculosis (TB). This test is intended as an aid in the diagnosis of pulmonary tuberculosis when used in conjunction with clinical and other laboratory findings.** The GeneXpert MTB/RIF Assay must also be used in conjunction with mycobacterial culture to address the risk of false negative results and to recover the organisms for further characterization and drug susceptibility testing.

Sample Criteria

Sputum samples (raw sputum or concentrated sediments prepared from induced or expectorated sputum) from a patient with first time positive acid-fast bacilli (AFB) sputum-smear results will be tested with the GeneXpert MTB/RIF assay. Exceptions to this protocol include:

- grossly bloody specimens,
- non-sputum specimens (e.g., blood, CSF, gastric aspirate, stool, tissue, urine, etc.) except for specimens obtained by BAL ,
- patients that have been treated for *M. tuberculosis* complex within the last year,
- patients that have been on anti-tuberculosis treatment or have been on therapy more than 3 days prior to collection of the specimen.

Sample Storage

- Sputum specimens may be stored for a maximum of 3 days at room temperature (maximum temperature not to exceed 35°C or 95°F) or up to 10 days at refrigerated (2-8°C) temperature from collection.
- Sputum sediment may be stored up to 7 days from collection at refrigerator (2-8°C) temperature.

Testing

Testing will be performed within 24 hours from the time a positive AFB sputum-smear result is reported. Please contact the DLS TB lab at 502-564-4446 x 4422 or 4423 **as soon as possible** if a sample is anticipated to arrive to the DLS in the mid to late afternoon. This advance notification will help the TB staff in their planning on whether to perform the test beyond the standard operating hours of 8 AM until 4:30 PM (Eastern Time Zone) and to prepare necessary reagents/supplies for GeneXpert MTB/RIF assay testing.

Specimens from patients with negative AFB sputum-smear results are not routinely tested by the GeneXpert MTB/RIF assay. Medical providers should contact the State TB program for consultation concerning testing of patients with negative AFB sputum-smear results and with signs and symptoms of active TB disease. The State TB program will discuss criteria and provide guidance on a case-to-case basis with the submitter and will gladly provide consultation on any suspected TB case. Only smear negative specimens approved through the state TB Program will be tested. If approved, three early morning or induced sputum specimens may be sent to DLS. The sensitivity of the GeneXpert MTB/RIF assay for detection of *M. tuberculosis* from AFB-smear negative specimens is 76.1%.

State TB Program contacts

- Maria Dalbey, RN, BSN; Maria.Dalbey@ky.gov, Ph: 502-564-4276 x4292, Fax: 502-564-3772
- Emily Anderson RN, BSN; EmilyA.Anderson@ky.gov, Ph: 502-564-4276 x 4298
- Robert L. Brawley, MD, MPH, FSHEA), Robert.Brawley@ky.gov, Ph: 502-564-3261 x4235

Limitations

- GeneXpert MTB/RIF Assay is not a test of cure and should not be performed on patients who have received more than 3 days of treatment. Previously treated patients must be off anti-tuberculosis therapy for at least 1 year for valid testing.
- A negative test does not exclude the possibility of isolating MTB-complex from the sputum sample. The GeneXpert MTB/RIF Assay must be used in conjunction with mycobacterial culture to address the risk of false negative results and to recover the organism for further characterization and susceptibility testing.
- A positive test does not necessarily indicate the presence of viable organisms.
- The GeneXpert MTB/RIF Assay does not differentiate between the species of the MTB-complex (e.g., *Mycobacterium tuberculosis*, *M. africanum*, *M. bovis*, *M. bovis* BCG, *M. canettii*, *M. caprae*, *M. microti*, or *M. pinnipedii)*
- **Because the detection of MTB-complex is dependent on the number of organisms present in the sample, accurate results are dependent on proper specimen collection, handling, and storage. Erroneous test results might occur from improper specimen collection**
- The performance of the GeneXpert MTB/RIF Assay has not been evaluated with samples from pediatric patients.

- The test is FDA approved only for sputum specimens (induced or non-induced). Testing on other respiratory specimens (e.g., BAL) will be reported with a disclaimer. No other specimens will be tested by this method.

INTERFERING SUBSTANCES

Potential inhibitory effects of substances that may be present in samples processed with the GeneXpert MTB/RIF Assay include, but are not limited to, blood, pus, mammalian cells, and hemoglobin. Interference may be observed in the presence of Lidocaine (>20% v/v), mucin (>1.5% w/v), Ethambutol (>5 µg/mL), Guaifenesin (>2.5 mg/mL), Phenylephrine (>25% v/v), or tea tree oil (>0.008% v/v).

Note: Please call the TB Lab for any questions or guidance on entering any TB testing request orders in the DLS Psyche Outreach LIMS System. Please include thorough patient clinical history and administration of any current and past drug treatment for tuberculosis. **When entering orders for patient specimens in Outreach it is important to search for previous orders** on that particular patient. If the patient has previous orders, select that patient to bring up all the patient demographics onfile and proceed with edit clinical order. This links the patient data that is crucial for patient history, surveillance, and tracking patient results. This information is helpful for the state TB program and for the DLS lab to better serve the patient and submitter in public health's goals of expedited treatment, TB control, and in the national and global efforts to eliminate TB.

Sources:

- http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6241a1.htm?s_cid=mm6241a1_e
- Xpert MTB/RIF assay [package insert]. Sunnydale, CA: Cepheid; 2013

Managing Laboratory Data

- The LHD shall ensure that all culture positive pulmonary and extrapulmonary *Mycobacterium tuberculosis* isolates from outside laboratories are sent to the State Public Health Laboratory for drug susceptibility and genotype testing. Per the amendments to the Kentucky regulation, "902 KAR 2:020, Reportable disease surveillance," http://www.lrc.ky.gov/kar/902/002/020.htm, "A medical or national reference laboratory shall submit clinical isolates or, if not available, the direct specimen from" tuberculosis cases to the Division of Laboratory Services (i.e., the State Public Health Laboratory). The amended regulation became effective on February 26, 2015.

- The LHD shall ensure that copies of sputum positive TB culture results, positive TB culture results from any other body site, and positive results for Nucleic Acid Amplification tests (e.g., MTD positive results and PCR positive results) from outside laboratories are sent to the State TB Prevention and Control Program. Copies should be sent to the Kentucky TB Program within one (1) business day of being received by LHD TB Coordinators.

- It is the responsibility of the LHD to ensure that drug susceptibility testing is performed on initial culture positive pulmonary and extrapulmonary TB isolates. Send a copy of the laboratory report about drug susceptibility testing to the State TB Prevention and Control Program. Outside laboratories that report culture positive pulmonary and extrapulmonary TB isolates may need an additional physician order to perform drug susceptibility testing.

- It is recommended that all sputum samples be sent to the State Public Health Lab for testing.

GUIDELINES FOR FOLLOW-UP NOTIFICATION

For active TB cases, suspects, contacts to cases, and individuals receiving directly observed preventive therapy, LHDs shall make at least three attempts to notify patients / parents of missed appointments, abnormal laboratory or radiology tests as follows:

1. Initial contact may be made by telephone if the number is available.

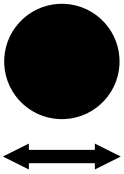
2. The second contact should be a regular mailed letter with directions for the patient to contact the LHD for follow-up.

3. The third contact should be a certified or registered letter with directions for the patient to contact the LHD for follow-up. The letter receipt shall be retained or scanned in the patient's medical record.

4. If the patient cannot be contacted by the above measures, a face-to-face visit shall be attempted.

5. If after three of the above measures are made with no response, the LHD should document in the medical record that the patient is lost to follow-up care and notify the KY TB Program for additional guidance.

CLASSIFYING THE TUBERCULIN SKIN TEST REACTION

 5 or More Millimeters	 10 or More Millimeters	 15 or More Millimeters
≥ 5 mm is classified as positive in: • HIV-positive persons • Recent contacts of a case with active TB disease • People who have previously had active TB disease • Persons with fibrotic changes on chest radiograph consistent with old healed TB • Patients with organ transplants and other immunosuppressed patients (including patients taking a prolonged course of oral or intravenous corticosteroids or tumor necrosis factor alpha (TNF-alpha) antagonists)	≥ 10 mm is classified as positive in: • People who have come to the U.S. within the last 5 years from areas of the world where TB is common * • Injection drug users • People who live or work in high-risk congregate settings • Mycobacteriology laboratory personnel • Children younger than 4 years • Infants, children, and adolescents exposed to adults in high-risk categories** • Persons with clinical conditions that place them at high-risk for TB (silicosis, diabetes mellitus, severe kidney disease, certain types of cancer, and certain intestinal conditions)	≥ 15 mm is classified as positive in: • Persons with no known risk factors for TB • Targeted skin testing programs should only be conducted among high-risk groups

A tuberculin skin test conversion is defined as an increase of ≥ 10 mm of induration within a 2-year period, regardless of age.

ATS Diagnostic Standards and Classification of Tuberculosis in Adults and Children. Am. J. Respir. Care Med., 4/00

Core Curriculum on Tuberculosis; What the Clinician Should Know (2013).

*See tables with international TB incidence and prevalence rates in this reference for more information.

**According to Red Book, 2012, ≥10 mm induration is considered positive for children with increased exposure to adults who are HIV-infected, homeless, users of illicit drugs, residents of nursing homes, incarcerated or migrant farm workers, p. 680.

"TUBERCULIN SKIN TEST (TST) RECOMMENDATIONS FOR INFANTS, CHILDREN, AND ADOLESCENTS[1]

Children for whom immediate TST or IGRA is indicated[2]:

- Contacts of people with confirmed or suspected contagious [active] tuberculosis [disease] (contact investigation)
- Children with radiographic or clinical findings suggesting [active] tuberculosis disease
- Children immigrating from countries with endemic infection (e.g., Asia, Middle East, Africa, Latin America, countries of the former Soviet Union) including international adoptees
- Children with travel histories to countries with endemic infection and substantial contact with indigenous persons from such countries[3]

Children who should have annual TST or IGRA:

- Children infected with HIV infection (TST only)
- Incarcerated adolescents

Children at increased risk of progression of LTBI to tuberculosis disease: Children with other medical conditions, including diabetes mellitus, chronic renal failure, malnutrition, and congenital or acquired immunodeficiency's deserve special consideration. Without recent exposure, these people are not at increased risk of acquiring tuberculosis infection. Underlying immune deficiencies associated with these conditions theoretically would enhance the possibility for progression to severe disease. Initial histories of potential exposure to tuberculosis should be included for all of these patients. If these histories or local epidemiologic factors suggest a possibility of exposure, immediate and periodic TST or IGRA should be considered. **An initial TST or IGRA should be performed before initiation of immunosuppressive therapy, including prolonged steroid administration, use of tumor necrosis factor-alpha antagonists, or other immunosuppressive therapy in any child requiring these treatments."**

A TST can be administered to individuals of any age who are at increased risk for acquiring LTBI or active TB disease, even to newborn infants (See Congenital Tuberculosis in the 2012 edition of the Red Book, p. 754.).

IGRA indicates interferon-gamma release assay; HIV indicates human immunodeficiency virus; LTBI, latent tuberculosis infection.

[1] Bacille Calmette-Guérin immunization is not a contraindication to a TST.

[2] Beginning as early as 3 months of age.

[3] If the child is well, the TST or IGRA should be delayed for up to 10 weeks after return.

Reference: Red Book 2012

INDICATIONS FOR TWO-STEP TUBERCULIN SKIN TESTS (TSTs)

Situation	Recommended testing
No previous TST result	Two-step baseline TSTs
Previous negative TST result (documented or not) >12 months before new employment	Two-step baseline TSTs
Previous documented negative TST result ≤12 months before new employment	Single TST needed for baseline testing; this test will be the second-step
≥2 previous documented negative TSTs but most recent TST >12 months before new employment	Single TST; two-step testing is not necessary
Previous documented positive TST result	No TST
Previous undocumented positive TST result*	Two-step baseline TST(s)
Previous BCG† vaccination	Two-step baseline TST(s)
Programs that use serial BAMT,§ including QFT¶ (or the previous version QFT)	See Supplement, Use of QFT-G** for Diagnosing *M. tuberculosis* Infections in Health-Care Workers (HCWs)

* For newly hired health-c are workers and other persons who will be tested on a routine basis (e.g., residents or staff of correctional or long-term–care facilities), a previous TST is not a contraindication to a subsequent TST, unless the test was associated with severe ulceration or anaphylactic shock, which are substantially rare adverse events. If the previous positive TST result is not documented, administer two-step TSTs or offer BAMT. **SOURCES:** Aventis Pasteur. Tuberculin purified protein derivative (Mantoux) Tubersol® diagnostic antigen. Toronto, Ontario, Canada: Aventis Pasteur; 2001. Parkdale Pharmaceuticals. APLISOL (Tuberculin purified protein derivative, diluted [stabilized solution]). Diagnostic antigen for intradermal injection only. Rochester, MI: Parkdale Pharmaceuticals; 2002. Froeschle JE, Ruben FL, Bloh AM. Immediate hypersensitivity reactions after use of tuberculin skin testing. Clin Infect Dis 2002;34:E12–3.

† Bacille Calmette-Guérin.

§ Blood assay for *Mycobacterium tuberculosis.*

¶ QuantiFERON®-TB test.

** QuantiFERON®-TB Gold test.

MMWR Guidelines for Preventing the Transmission of Mycobacterium tuberculosis in Health-Care settings, 2005, p 29.

I. MANAGEMENT OF TUBERCULOSIS DISEASE

BOX 2. Risk factors for progression of infection to active tuberculosis

Persons at increased risk* for progression of infection to active tuberculosis include

- persons with human immunodeficiency virus (HIV) infection;†
- infants and children aged <5 years;†
- persons who are receiving immunosuppressive therapy such as tumor necrosis factor--alpha (TNF-α) antagonists, systemic corticosteroids equivalent to ≥15 mg of prednisone per day, or immune suppressive drug therapy following organ transplantation;†
- persons who were recently infected with *M. tuberculosis* (within the past 2 years);
- persons with a history of untreated or inadequately treated active tuberculosis, including persons with fibrotic changes on chest radiograph consistent with prior active tuberculosis;
- persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, or cancer of the head, neck, or lung;
- persons who have had a gastrectomy or jejunoileal bypass;
- persons who weigh <90% of their ideal body weight;
- cigarette smokers and persons who abuse drugs or alcohol; and
- populations defined locally as having an increased incidence of active tuberculosis, possibly including medically underserved or low-income populations

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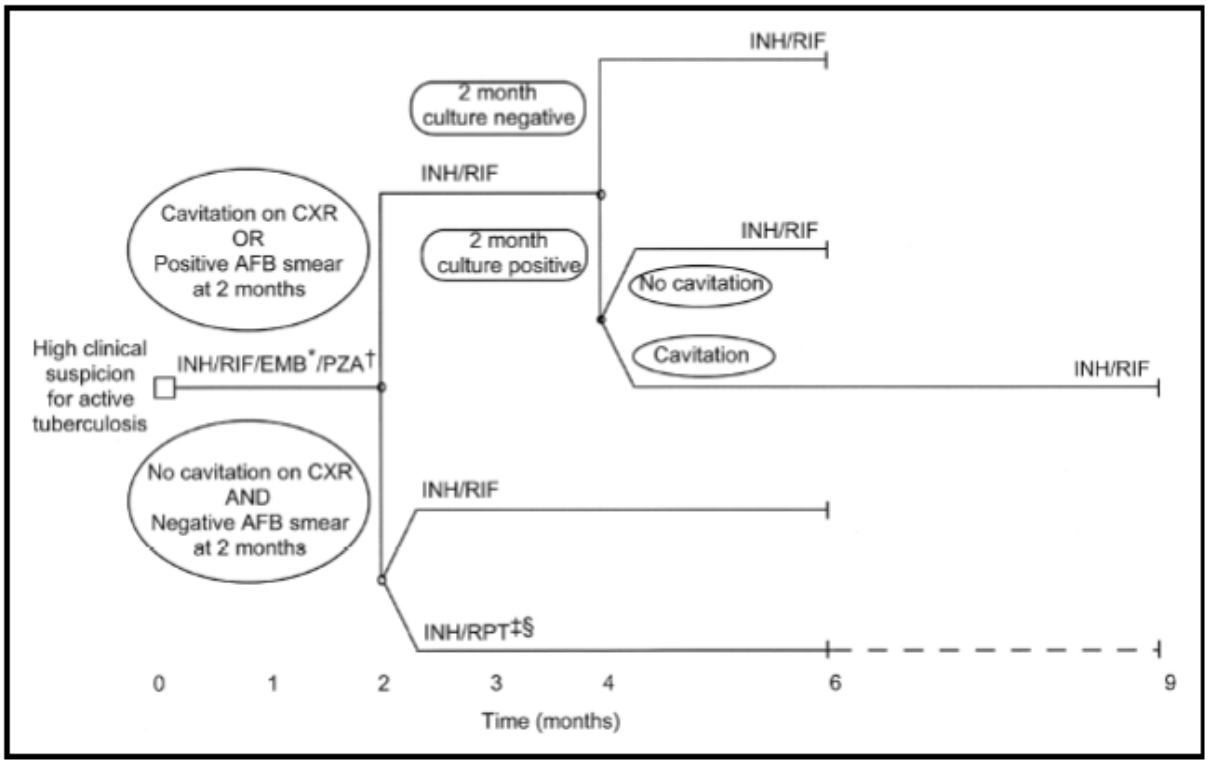
Source: Based on CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6).

* Persons with these characteristics have an increased risk for progression of infection to active tuberculosis compared with persons without these characteristics.

† Indicates persons at increased risk for a poor outcome (e.g., meningitis, disseminated disease, or death) if active tuberculosis occurs.

Treatment Algorithm for Culture-Positive Tuberculosis

FIGURE 1. Treatment algorithm for tuberculosis.



Patients in whom tuberculosis is proved or strongly suspected should have treatment initiated with isoniazid, rifampin, pyrazinamide, and ethambutol for the initial 2 months. A repeat smear and culture should be performed when 2 months of treatment has been completed. If cavities were seen on the initial chest radiograph or the acid-fast smear is positive at completion of 2 months of treatment, the continuation phase of treatment should consist of isoniazid and rifampin daily or twice weekly for 4 months to complete a total of 6 months of treatment. If cavitation was present on the initial chest radiograph and the culture at the time of completion of 2 months of therapy is positive, the continuation phase should be lengthened to 7 months (total of 9 months of treatment). If the patient has HIV infection and the $CD4^+$ cell count is <100/µl, the continuation phase should consist of daily or three times weekly isoniazid and rifampin. In HIV-uninfected patients having no cavitation on chest radiograph and negative acid-fast smears at completion of 2 months of treatment, the continuation phase may consist of either once weekly isoniazid and rifapentine, or daily or twice weekly isoniazid and rifampin, to complete a total of 6 months (bottom). Patients receiving isoniazid and rifapentine, and whose 2-month cultures are positive, should have treatment extended by an additional 3 months (total of 9 months).

* EMB may be discontinued when results of drug susceptibility testing indicate no drug resistance.

† PZA may be discontinued after it has been taken for 2 months (56 doses).

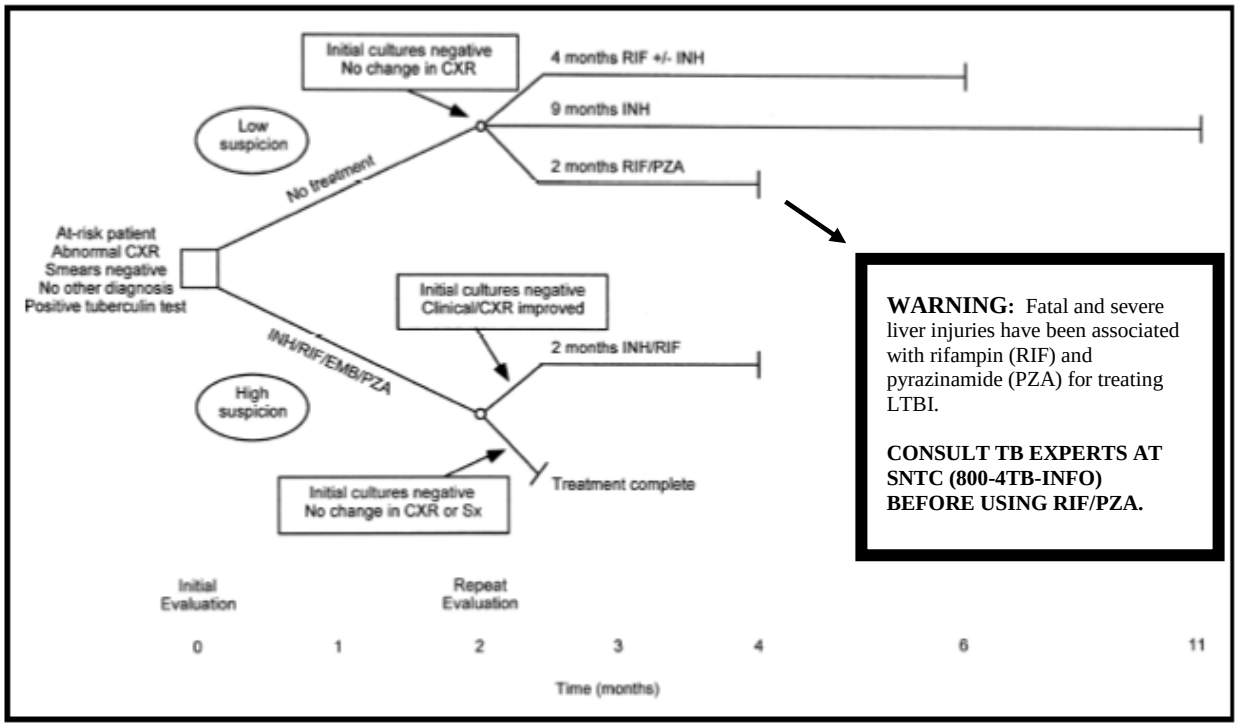
‡ RPT should not be used in HIV-infected patients with tuberculosis or in patients with extrapulmonary tuberculosis.

§ Therapy should be extended to 9 months if 2-month culture is positive.

CXR = chest radiograph; EMB = ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003;52(No. RR-11): 6.

Treatment Algorithm for Active, Culture-negative Pulmonary Tuberculosis and Inactive Tuberculosis



The decision to begin treatment for a patient with sputum smears that are negative depends on the degree of suspicion that the patient has tuberculosis. The considerations in choosing among the treatment options are discussed in text. If the clinical suspicion is high (bottom), then multidrug therapy should be initiated before acid-fast smear and culture results are known. If the diagnosis is confirmed by a positive culture, treatment can be continued to complete a standard course of therapy (see Figure 1). If initial cultures remain negative and treatment has consisted of multiple drugs for 2 months, then there are two options depending on repeat evaluation at 2 months (bottom): 1) if the patient demonstrates symptomatic or radiographic improvement without another apparent diagnosis, then a diagnosis of culture-negative tuberculosis can be inferred. Treatment should be continued with isoniazid and rifampin alone for an additional 2 months; 2) if the patient demonstrates neither symptomatic nor radiographic improvement, then prior tuberculosis is unlikely and treatment is complete once treatment including at least 2 months of rifampin and pyrazinamide has been administered. In low-suspicion patients not initially receiving treatment (top), if cultures remain negative, the patient has no symptoms, and the chest radiograph is unchanged at 2–3 months, there are three treatment options: these are 1) isoniazid for 9 months, 2) rifampin with or without isoniazid for 4 months, or 3) rifampin and pyrazinamide for 2 months. CXR = chest X-ray; EMB = ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; Sx = signs/symptoms. (It should be noted that the RIF/PZA 2-month regimen should be used only for patients who are not likely to complete a longer course of treatment and can be monitored closely.)

Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003;52(No. RR-11): 7.

DIRECTLY OBSERVED THERAPY (DOT)

DOT is a method of ensuring patients' adherence to therapy. LHD staff must recognize DOT as the Kentucky standard of care. All active TB disease, whether pulmonary or extrapulmonary, shall be treated by DOT. The DOT method must be conveyed with confidence to patients. Always respect the patient's confidentiality.

The Centers for Disease Control and Prevention (CDC) and the American Thoracic Society (ATS) recommends that all TB patients be considered for DOT because of the difficulty in predicting who will adhere to the treatment regimen.

The following persons must be placed on DOT for treatment of tuberculosis:

- All patients being treated for suspected pulmonary or extrapulmonary TB.
- All patients diagnosed with culture positive pulmonary and or extrapulmonary TB.
- All patients diagnosed as a "clinical case" of pulmonary TB or extrapulmonary TB because of negative TB cultures but who had chest x-ray and / or clinical improvement on antiTB therapy.

DOT means that a specially trained health department health care professional, not related to the patient, watches the patient swallow each dose of TB medication. DOT is never to be delegated to a family member. Kentucky's TB Control Program does not consider nor count the dosage as DOT if a family observes the patient taking the medication. Such actions could result in prolonged treatment and be considered noncompliance with the DOT agreement.

Be aware of techniques a patient may use to avoid swallowing the medication such as hiding the pills in the mouth, spitting the pills into the fluid used to take them with, or vomiting the pills after leaving the treatment site.

DOT reduces the frequency of treatment failures, of acquiring drug resistance, and in suffering relapse of the disease. Intermittent DOT reduces the total number of doses a patient must take and the number of encounters with LHD personnel. If the patient cannot go to a LHD, LHD staff can arrange another site that is safe, convenient, and agreeable to both patient and staff.

Besides being cost effective, DOT has many other benefits. DOT is a patient-focused service that also provides the health care worker with a better understanding of the patient's needs, thus placing the worker in position to assist with needed health or social services, and making the appropriate referrals. DOT provides an effective opportunity for education, not only of the patient but also of the patient's support system. DOT is also advantageous to the community because a patient on DOT becomes noninfectious much more quickly. This reduces the time that a patient is able to spread the disease in the community.

KY V-DOT
Video Directly Observed Therapy

Directly observed therapy (DOT) for tuberculosis increases patient adherence. This increased adherence both reduces the risk of disease recurrence and prevents the development of resistant *Mycobacterium tuberculosis* strains.

Once the patient has completed eight (8) weeks of medication by DOT (initial phase), video DOT is an option. Video DOT is an option in place of at home/office DOT that local health departments can offer to patients.

During Video DOT, the local health department determines a supply of pre-packaged medication doses that will be given to the patient at each clinic visit. The local health department personnel will arrange a set time for the remote video call with the patient**.** During the video call, the patient will be expected to display the medications onscreen*. The health worker will then witness the patient swallowing the medication.

All patients participating must agree to the requirements of the Video DOT program and sign a consent form.

See TB Program teaching sheet **TB-14a for Video DOT protocols and consent form **TB-14b**.*

Exclusion Criteria for Video DOT

- Patient in isolation.
- Patient with side effects requiring graduated doses.
- Illegal activities occurring in the home.
- Video DOT must be accomplished within 15 minutes.
- Lack of stable environment or lack of telephone at patient location.
- Less than 90% compliance with therapy during the initial eight (8) weeks of standard DOT.
- Less than 90% compliance with the treatment regimen or scheduled Video DOT appointments
- Inability to maintain effective communication via the video call either due to patient disability or language barriers.
- Inability of the patient to demonstrate effective use of the equipment.
- MDR TB

DRUG REGIMENS FOR MICROBIOLOGICALLY CONFIRMED PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS

Preferred Regimen from 2016 Treatment Guidelines:

Intensive Phase		Continuation Phase			
Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]
INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	7 d/wk for 126 doses (18 wk), or 5 d/wk for 90 doses (18 wk)	182–130	This is the preferred regimen for patients with newly diagnosed pulmonary tuberculosis.

Preferred Alternative Regimen from 2016 Treatment Guidelines;

Intensive Phase		Continuation Phase			
Drug[a]	Interval and Dose[b] (Minimum Duration)	Drugs	Interval and Dose[b,c] (Minimum Duration)	Range of Total Doses	Comments[c,d]
INH RIF PZA EMB	7 d/wk for 56 doses (8 wk), or 5 d/wk for 40 doses (8 wk)	INH RIF	3 times weekly for 54 doses (18 wk)	110–94	Preferred alternative regimen in situations in which more frequent DOT during continuation phase is difficult to achieve.

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB, Clin Infect Dis. 2016; 63:4

DRUG REGIMENS FOR MICROBIOLOGICALLY CONFIRMED PULMONARY TUBERCULOSIS CAUSED BY DRUG-SUSCEPTIBLE ORGANISMS (Continued)

Footnotes for 2016 Treatment Regimens on page 21:

Abbreviations: DOT, directly observed therapy; EMB, ethambutol; HIV, human immunodeficiency virus; INH, isoniazid; PZA, pyrazinamide; RIF, rifampin.

[a] Other combinations may be appropriate in certain circumstances; additional details are provided in the section "Recommended Treatment Regimens."

[b] When DOT is used, drugs may be given 5 days per week and the necessary number of doses adjusted accordingly. Although there are no studies that compare 5 with 7 daily doses, extensive experience indicates this would be an effective practice. DOT should be used when drugs are administered <7 days per week.

[c] Based on expert opinion, patients with cavitation on initial chest radiograph and positive cultures at completion of 2 months of therapy should receive a 7-month (31-week) continuation phase.

[d] Pyridoxine (vitamin B6), 25–50 mg/day, is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/day.

Alternative Regimen from 2003 Treatment Guidelines

Initial phase		Continuation phase			Range of total doses (minimal duration)
Drugs	Interval and doses‡ (minimal duration)	Regimen	Drugs	Interval and doses‡§ (minimal duration)	
INH RIF PZA EMB	Seven days per week for 56 doses (8 wk) or 5 d/wk for 40 doses (8 wk)¶	1a	INH/RIF	Seven days per week for 126 doses (18 wk) or 5 d/wk for 90 doses (18 wk)¶	182–130 (26 wk)
		1b	INH/RIF	Twice weekly for 36 doses (18 wk)	92–76 (26 wk)

Definition of abbreviations: EMB = Ethambutol; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; RPT = rifapentine.

Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003;52(No. RR-11): 3.

DOSES[a] OF ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN[b]

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
First-line drugs						
Isoniazid	Tablets (50 mg, 100 mg, 300 mg); elixir (50 mg/5 mL); aqueous solution (100 mg/mL) for intravenous or intramuscular injection. Note: Pyridoxine (vitamin B6), 25–50 mg/day, is given with INH to all persons at risk of neuropathy (eg, pregnant women; breastfeeding infants; persons with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or patients with advanced age). For patients with peripheral neuropathy, experts recommend increasing pyridoxine dose to 100 mg/d.	Adults	5 mg/kg (typically 300 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (typically 900 mg)	15 mg/kg (typically 900 mg)
		Children	10–15 mg/kg	. . .	20–30 mg/kg	. . .[b]
Rifampin	Capsule (150 mg, 300 mg). Powder may be suspended for oral administration. Aqueous solution for intravenous injection.	Adults[c]	10 mg/kg (typically 600 mg)	. . .	10 mg/kg (typically 600 mg)	10 mg/kg (typically 600 mg)
		Children	10–20 mg/kg	. . .	10–20 mg/kg	. . .[b]
Rifabutin	Capsule (150 mg)	Adults[d]	5 mg/kg (typically 300 mg)	. . .	Not recommended	Not recommended
		Children	Appropriate dosing for children is unknown. Estimated at 5 mg/kg.			
Rifapentine	Tablet (150 mg film coated)	Adults		10–20 mg/kg[e]	. . .	. . .
		Children	Active tuberculosis: for children ≥12 y of age, same dosing as for adults, administered once weekly. Rifapentine is not FDA-approved for treatment of active tuberculosis in children <12 y of age.			
Pyrazinamide	Tablet (500 mg scored)	Adults	See Table 10	. . .	See Table 10	See Table 10
		Children	35 (30–40) mg/kg	. . .	50 mg/kg	. . .[b]
Ethambutol	Tablet (100 mg; 400 mg)	Adults	See Table 11	. . .	See Table 11	See Table 11
		Children[f]	20 (15–25) mg/kg	. . .	50 mg/kg	. . .[b]

When using 2016 Treatment Guidelines, Any resistance to first or second line drugs, contact SNTC

ATS/CDC/IDSA Clinical Practice Guidelines for Drug-Susceptible TB, Clin Infect Dis. 2016; 63:5-6

DOSES[a] OF ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN[b] (Continued)

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
Second-line drugs						
Cycloserine	Capsule (250 mg)	Adults[g]	10–15 mg/kg total (usually 250–500 mg once or twice daily)	There are inadequate data to support intermittent administration.		
		Children	15–20 mg/kg total (divided 1–2 times daily)			
Ethionamide	Tablet (250 mg)	Adults[h]	15–20 mg/kg total (usually 250–500 mg once or twice daily)	There are inadequate data to support intermittent administration.		
		Children	15–20 mg/kg total (divided 1–2 times daily)			
Streptomycin	Aqueous solution (1 g vials) for IM or IV administration.	Adults	15 mg/kg daily. Some clinicians prefer 25 mg/kg 3 times weekly. Patients with decreased renal function may require the 15 mg/kg dose to be given only 3 times weekly to allow for drug clearance.			
		Children	15–20 mg/kg [427]	. . .	25–30 mg/kg[i]	. . .
Amikacin/ kanamycin	Aqueous solution (500 mg and 1 g vials) for IM or IV administration.	Adults	15 mg/kg daily. Some clinicians prefer 25 mg/kg 3 times weekly. Patients with decreased renal function, including older patients, may require the 15 mg/kg dose to be given only 3 times weekly to allow for drug clearance.			
		Children	15–20 mg/kg [427]	. . .	25–30 mg/kg[i]	. . .
Capreomycin	Aqueous solution (1 g vials) for IM or IV administration.	Adults	15 mg/kg daily. Some clinicians prefer 25 mg/kg 3 times weekly. Patients with decreased renal function, including older patients, may require the 15 mg/kg dose to be given only 3 times weekly to allow for drug clearance.			
		Children	15–20 mg/kg [427]	. . .	25–30 mg/kg[i]	. . .
Para-amino salicylic acid	Granules (4 g packets) can be mixed in and ingested with soft food (granules should not be chewed). Tablets (500 mg) are still available in some countries, but not in the United States. A solution for IV administration is available in Europe.	Adults	8–12 g total (usually 4000 mg 2–3 times daily)	There are inadequate data to support intermittent administration.		
		Children	200–300 mg/kg total (usually divided 100 mg/kg given 2 to 3 times daily)			

DOSES[a] OF ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN[b] (Continued)

Drug	Preparation	Population	Daily	Once-Weekly	Twice-Weekly	Thrice-Weekly
Levofloxacin	Tablets (250 mg, 500 mg, 750 mg); aqueous solution (500 mg vials) for IV injection.	Adults	500–1000 mg daily	There are inadequate data to support intermittent administration.		
		Children	The optimal dose is not known, but clinical data suggest 15–20 mg/kg [427]			
Moxifloxacin	Tablets (400 mg); aqueous solution (400 mg/250 mL) for IV injection	Adults	400 mg daily	There are inadequate data to support intermittent administration.[j]		
		Children	The optimal dose is not known. Some experts use 10 mg/kg daily dosing, though lack of formulations makes such titration challenging. Aiming for serum concentrations of 3–5 µL/mL 2 h postdose is proposed by experts as a reasonable target.			

Abbreviations: FDA, US Food and Drug Administration; HIV, human immunodeficiency virus; IM, intramuscular; INH, isoniazid; IV, intravenous.

[a] Dosing based on actual weight is acceptable in patients who are not obese. For obese patients (>20% above ideal body weight [IBW]), dosing based on IBW may be preferred for initial doses. Some clinicians prefer a modified IBW (IBW + [0.40 × (actual weight – IBW)]) as is done for initial aminoglycoside doses. Because tuberculosis drug dosing for obese patients has not been established, therapeutic drug monitoring may be considered for such patients.

[b] For purposes of this document, adult dosing begins at age 15 years or at a weight of >40 kg in younger children. The optimal doses for thrice-weekly therapy in children and adolescents have not been established. Some experts use in adolescents the same doses as recommended for adults, and for younger children the same doses as recommended for twice-weekly therapy.

[c] Higher doses of rifampin, currently as high as 35 mg/kg, are being studied in clinical trials.

[d] Rifabutin dose may need to be adjusted when there is concomitant use of protease inhibitors or nonnucleoside reverse transcriptase inhibitors.

[e] TBTC Study 22 used rifapentine (RPT) dosage of 10 mg/kg in the continuation phase of treatment for active disease [9]. However, RIFAQUIN and PREVENT TB safely used higher dosages of RPT, administered once weekly [164, 210]. Daily doses of 1200 mg RPT are being studied in clinical trials for active tuberculosis disease.

[f] As an approach to avoiding ethambutol (EMB) ocular toxicity, some clinicians use a 3-drug regimen (INH, rifampin, and pyrazinamide) in the initial 2 months of treatment for children who are HIV-uninfected, have no prior tuberculosis treatment history, are living in an area of low prevalence of drug-resistant tuberculosis, and have no exposure to an individual from an area of high prevalence of drug-resistant tuberculosis. However, because the prevalence of and risk for drug-resistant tuberculosis can be difficult to ascertain, the American Academy of Pediatrics and most experts include EMB as part of the intensive-phase regimen for children with tuberculosis.

[g] Clinicians experienced with using cycloserine suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations often are useful in determining the appropriate dose for a given patient. Few patients tolerate 500 mg twice daily.

[h] Ethionamide can be given at bedtime or with a main meal in an attempt to reduce nausea. Clinicians experienced with using ethionamide suggest starting with 250 mg once daily and gradually increasing as tolerated. Serum concentrations may be useful in determining the appropriate dose for a given patient. Few patients tolerate 500 mg twice daily.

[i] Modified from adult intermittent dose of 25 mg/kg, and accounting for larger total body water content and faster clearance of injectable drugs in most children. Dosing can be guided by serum concentrations.

[j] RIFAQUIN trial studied a 6-month regimen. Daily isoniazid was replaced by daily moxifloxacin 400 mg for the first 2 months, followed by once-weekly doses of moxifloxacin 400 mg and RPT 1200 mg for the remaining 4 months. Two hundred twelve patients were studied (each dose of RPT was preceded by a meal of 2 hard-boiled eggs and bread). This regimen was shown to be noninferior to a standard daily administered 6-month regimen [164].

DOSES* OF ANTITUBERCULOSIS DRUGS FOR ADULTS AND CHILDREN†
(Continued)

MMWR, June 20, 2003, p. 5

TABLE 4. Suggested pyrazinamide doses, using whole tablets, for adults weighing 40–90 kilograms

	Weight (kg)*		
	40–55	56–75	76–90
Daily, mg (mg/kg)	1,000 (18.2–25.0)	1,500 (20.0–26.8)	2,000† (22.2–26.3)
Thrice weekly, mg (mg/kg)	1,500 (27.3–37.5)	2,500 (33.3–44.6)	3,000† (33.3–39.5)
Twice weekly, mg (mg/kg)	2,000 (36.4–50.0)	3,000 (40.0–53.6)	4,000† (44.4–52.6)

*Based on estimated lean body weight.
†Maximum dose regardless of weight.

TABLE 5. Suggested ethambutol doses, using whole tablets, for adults weighing 40–90 kilograms

	Weight (kg)*		
	40–55	56–75	76–90
Daily, mg (mg/kg)	800 (14.5–20.0)	1,200 (16.0–21.4)	1,600† (17.8–21.1)
Thrice weekly, mg (mg/kg)	1,200 (21.8–30.0)	2,000 (26.7–35.7)	2,400† (26.7–31.6)
Twice weekly, mg (mg/kg)	2,000 (36.4–50.0)	2,800 (37.3–50.0)	4,000† (44.4–52.6)

*Based on estimated lean body weight.
†Maximum dose regardless of weight.

Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003;52(No. RR-11): 5.

PYRIDOXINE (VITAMIN B6) SUPPLEMENTATION DURING TREATMENT OF LTBI OR ACTIVE TB DISEASE

Prevention of Peripheral Neuropathy and Central Nervous Symptom Effects of INH

Indications for pyridoxine when INH is ordered to treat LTBI or active TB disease:

Adults: Pyridoxine supplementation can be ordered for any adult being treated with INH, unless there is a medical contraindication. Pyridoxine (vitamin B6) supplementation is particularly recommended when INH is used for treatment of LTBI or active TB disease in some adults with medical conditions where peripheral neuropathy is common, such as[1, 2, 3]:

- Nutritional deficiencies
- Diabetes
- HIV infection
- Chronic renal failure
- Alcoholism
- Persons with seizure disorders
- Pregnant women
- Breastfeeding women

Infants, children, and adolescents[1, 2, 3, 4, 5, 6]**:** Routine administration of pyridoxine is not recommended for most children and adolescents taking INH[4]. Pyridoxine is recommended when INH is used for treatment of LTBI or active TB disease in some infants, children, and adolescents at increased risk for peripheral neuritis or other INH adverse effects, such as:

- Breastfed infants, particularly those who are exclusively breastfed
- Children and adolescents on meat- and milk-deficient diets
- Children and adolescents with nutritional deficiencies
- Children who experience paresthesias while taking isoniazid
- HIV infection, particularly symptomatic HIV-infected individuals
- Pregnant adolescents
- Breastfeeding adolescents

Dose of pyridoxine when INH is ordered to treat LTBI or active TB disease:

Adults:

- CDC guidelines – 25 mg/day[1]
- Wisconsin TB Program guidelines – 10 to 50 mg/day[2]
- The Harriet Lane Handbook[5] – 25 to 100 mg/day

Infants, children, and adolescents:

- The Harriet Lane Handbook[5]: Child – 1-2 mg/kg/day. Pyridoxine injectable can be compounded with simple syrup to make an oral solution containing 1 mg/mL[6].
- 10 mg/day to 25 mg/day[1]

Prevention of Neurotoxic Effects of Cycloserine (A Second-line TB drug) in Adults:
Pyridoxine may help prevent and treat neurotoxic side effects of cycloserine in the treatment of active TB disease and is usually given in a dosage of 100--200 mg/day.[1]

Recommended Daily Allowances and Recommended Maximum Daily Intake[7]:
"The daily recommended dietary allowances (RDAs) of vitamin B6 are: Infants 0-6 months, 0.1 mg; Infants 7-12 months, 0.3 mg; Children 1-3 years, 0.5 mg; Children 4-8 years, 0.6 mg; Children 9-13 years, 1 mg; Males 14-50 years, 1.3 mg; Males over 50 years, 1.7 mg; Females 14-18 years, 1.2 mg; Females 19-50 years, 1.3 mg; Females over 50 years, 1.5 mg; Pregnant women, 1.9 mg; and breast-feeding women, 2 mg. Some researchers think the RDA for women 19-50 years should be increased to 1.5-1.7 mg per day. The recommended maximum daily intake is: Children 1-3 years, 30 mg; Children 4-8 years, 40 mg; Children 9-13 years, 60 mg; Adults, pregnant and breast-feeding women, 14-18 years, 80 mg; and Adults, pregnant and breast-feeding women, over 18 years, 100 mg."

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[1] Centers for Disease Control and Prevention. Treatment of Tuberculosis. MMWR 2003;52 (No. RR-11), http://www.cdc.gov/MMWR/PDF/rr/rr5211.pdf

[2] Centers for Disease Control and Prevention. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection. MMWR 2000;49(No. RR-6), http://www.cdc.gov/MMWR/PDF/rr/rr4906.pdf

[3] Wisconsin TB Program. "Frequently Asked Questions about Pyridoxine (Vitamin B-6)," http://www.dhs.wisconsin.gov/tb/resources/guidelines/pyridoxine_faq.pdf

[4] American Academy of Pediatrics. 2015 Red Book: Report of the Committee on Infectious Disease. Elk Grove Village, IL: American Academy of Pediatrics, p. 687.

[5] Robertson J, Shilkofski, N, editors. The Harriet Lane Handbook: A Manual for Pediatric House Officers, 17th Edition, Elsevier Mosby, 2005 p. 949.

[6] Nationwide Children's Hospital, Columbus OH. Pyridoxine Hydrochloride Oral Solution, http://www.nationwidechildrens.org/Document/Get/79362, accessed Nov 08, 2010.

[7] National Institutes of Health. Medline Plus: Pyridoxine (Vitamin B6), http://www.nlm.nih.gov/medlineplus/druginfo/natural/934.html, accessed Nov 08, 2010.

DOSAGE CHART*

Weight in Pounds	Weight in Kilograms	Dosage at 5 mg/kg	Dosage at 10 mg/kg	Dosage at 15 mg/kg	Dosage at 20 mg/kg	Dosage at 25 mg/kg	Dosage at 30 mg/kg
5	2.3	11.3	22.7	34.0	45.4	56.7	68.0
10	4.5	22.7	45.4	68.0	90.7	113.4	136.1
15	6.8	34.0	68.0	102.1	136.1	170.1	204.1
20	9.1	45.4	90.7	136.1	181.4	226.8	272.2
25	11.3	57	113	170	227	283	340
30	13.6	68	136	204	272	340	408
35	15.9	79	159	238	318	397	476
40	18.1	91	181	272	363	454	544
45	20.4	102	204	306	408	510	612
50	22.7	113	227	340	454	567	680
55	24.9	125	249	374	499	624	748
60	27.2	136	272	408	544	680	816
65	29.5	147	295	442	590	737	885
70	31.8	159	318	476	635	794	953
75	34.0	170	340	510	680	850	1021
80	36.3	181	363	544	726	907	1089
85	38.6	193	386	578	771	964	1157
90	40.8	204	408	612	816	1021	1225
95	43.1	215	431	646	862	1077	1293
100	45.4	227	454	680	907	1134	1361
105	47.6	238	476	714	953	1191	1429
110	49.9	249	499	748	998	1247	1497
115	52.2	261	522	782	1043	1304	1565
120	54.4	272	544	816	1089	1361	1633
125	56.7	283	567	850	1134	1417	1701
130	59.0	295	590	885	1179	1474	1769
135	61.2	306	612	919	1225	1531	1837
140	63.5	318	635	953	1270	1588	1905
145	65.8	329	658	987	1315	1644	1973
150	68.0	340	680	1021	1361	1701	2041
155	70.3	352	703	1055	1406	1758	2109
160	72.6	363	726	1089	1451	1814	2177
165	74.8	374	748	1123	1497	1871	2245
170	77.1	386	771	1157	1542	1928	2313
175	79.4	397	794	1191	1588	1984	2381
180	81.6	408	816	1225	1633	2041	2449
185	83.9	420	839	1259	1678	2098	2517
190	86.2	431	862	1293	1724	2155	2585
195	88.5	442	885	1327	1769	2211	2654
200	90.7	454	907	1361	1814	2268	2722
205	93.0	465	930	1395	1860	2325	2790
210	95.3	476	953	1429	1905	2381	2858
215	97.5	488	975	1463	1950	2438	2926
220	99.8	499	998	1497	1996	2495	2994
225	102.1	510	1021	1531	2041	2551	3062
230	104.3	522	1043	1565	2087	2608	3130
235	106.6	533	1066	1599	2132	2665	3198
240	108.9	544	1089	1633	2177	2722	3266
245	111.1	556	1111	1667	2223	2778	3334
250	113.4	567	1134	1701	2268	2835	3402

*Dosage calculated may have to be adjusted in order not to exceed the maximum dose for any drug being used.
Table recalculated in November 2010 with conversion factor of "1 pound = 0.45359237 kilograms."

Clinically Significant Drug–Drug Interactions Involving the Rifamycins[a]

Drug Class	Drugs Whose Concentrations Are Substantially Decreased by Rifamycins	Comments
Antiretroviral agents	HIV-1 protease inhibitors (lopinavir/ritonavir, darunavir/ritonavir, atazanavir, atazanavir/ritonavir)	RFB preferred with protease inhibitors. For ritonavir-boosted regimens, give RFB 150 mg daily. Double-dose lopinavir/ritonavir can be used with RIF but toxicity increased. Do not use RIF with other protease inhibitors.
	NNRTIs Nevirapine Efavirenz Rilpivirine Complera (fixed-dose combination tablet containing emtricitabine, rilpivirine, TDF) Etravirine	RIF decreases exposure to all NNRTIs. If nevirapine is used with RIF, lead-in nevirapine dose of 200 mg daily should be omitted and 400 mg daily nevirapine dosage given. With RIF, many experts advise that efavirenz be given at standard dosage of 600 mg daily, although FDA recommends increasing efavirenz to 800 mg daily in persons >60 kg. In young children double-dose lopinavir/ritonavir given with RIF results in inadequate concentrations – super-boosted Lopinavir/ritonavir is advised (if available) by some experts. Rilpivirine and etravirine should not be given with RIF. RFB can be used with nevirapine and etravirine at usual dosing. Efavirenz and RFB use requires dose increase of RFB to 600 mg daily, as such RIF is preferred. Rilpivirine should not be given with RFB.
	INSTIs Raltegravir Dolutegravir Elvitegravir (coformulated with cobicistat, tenofovir and emtricitabine as Stribild) Genvoya (fixed-dose combination tablet containing elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide)	Increase dose of raltegravir to 800 mg twice daily with RIF, although clinical trial data show similar efficacy using 400 mg twice daily. Dolutegravir dose should be increased to 50 mg every 12 h with RIF. Do not use RIF with elvitegravir. RFB can be used with all INSTIs.
	CCR5 inhibitors Maraviroc	RIF should not be used with maraviroc. RFB can be used with maraviroc.
Anti-infectives	Macrolide antibiotics (azithromycin, clarithromycin, erythromycin)	Azithromycin has no significant interaction with rifamycins. Coadministration of clarithromycin and RFB results in significant bidirectional interactions that can increase RFB to toxic levels increasing the risk of uveitis. Erythromycin is a CYP3A4 substrate and clearance may increase in setting of rifamycin use.
	Doxycycline	May require use of a drug other than doxycycline.
	Azole antifungal agents (ketoconazole, itraconazole, voriconazole, fluconazole, posaconazole, isavuconazole)	Itraconazole, ketoconazole, and voriconazole concentrations may be subtherapeutic with any of the rifamycins. Fluconazole can be used with rifamycins, but the dose of fluconazole may have to be increased.
	Atovaquone	Consider alternate form of *Pneumocystis jirovecii* treatment or prophylaxis.
	Chloramphenicol	Consider an alternative antibiotic.
	Mefloquine	Consider alternate form of malaria prophylaxis.

Clinically Significant Drug-Drug Interactions Involving the Rifamycins[a] (Continued)

Drug Class	Drugs Whose Concentrations Are Substantially Decreased by Rifamycins	Comments
Hormone therapy	Ethinylestradiol, norethindrone	Women of reproductive potential on oral contraceptives should be advised to add a barrier method of contraception when on a rifamycin.
	Tamoxifen	May require alternate therapy or use of a non-rifamycin-containing regimen.
	Levothyroxine	Monitoring of serum TSH recommended; may require increased dose of levothyroxine.
Narcotics	Methadone	RIF and RPT use may require methadone dose increase. RFB infrequently causes methadone withdrawal.
Anticoagulants	Warfarin	Monitor prothrombin time; may require 2- to 3-fold warfarin dose increase.
Immunosuppressive agents	Cyclosporine, tacrolimus	RFB may allow concomitant use of cyclosporine and a rifamycin; monitoring of cyclosporine and tacrolimus serum concentrations may assist with dosing.
	Corticosteroids	Monitor clinically; may require 2- to 3-fold increase in corticosteroid dose.
Anticonvulsants	Phenytoin, lamotrigine	TDM recommended; may require anticonvulsant dose increase.
Cardiovascular agents	Verapamil, nifedipine, diltiazem (a similar interaction is also predicted for felodipine and nisoldipine)	Clinical monitoring recommended; may require change to an alternate cardiovascular agent.
	Propranolol, metoprolol	Clinical monitoring recommended; may require dose increase or change to an alternate cardiovascular drug.
	Enalapril, losartan	Monitor clinically; may require a dose increase or use of an alternate cardiovascular drug.
	Digoxin (among patients with renal insufficiency), digitoxin	TDM recommended; may require digoxin or digitoxin dose increase.
	Quinidine	TDM recommended; may require quinidine dose increase.
	Mexiletine, tocainide, propafenone	Clinical monitoring recommended; may require change to an alternate cardiovascular drug.
Theophylline	Theophylline	TDM recommended; may require theophylline dose increase.
Sulfonylurea hypoglycemics	Tolbutamide, chlorpropamide, glyburide, glimepiride, repaglinide	Monitor blood glucose; may require dose increase or change to an alternate hypoglycemic drug.
Hypolipidemics	Simvastatin, fluvastatin	Monitor hypolipidemic effect; may require use of an alternate antihyperlipidemic drug.

Clinically Significant Drug-Drug Interactions Involving the Rifamycins[a] (Continued)

Drug Class	Drugs Whose Concentrations Are Substantially Decreased by Rifamycins	Comments
Psychotropic drugs	Nortriptyline	TDM recommended; may require dose increase or change to alternate psychotropic drug.
	Haloperidol, quetiapine	Monitor clinically; may require a dose increase or use of an alternate psychotropic drug.
	Benzodiazepines (eg, diazepam, triazolam), zolpidem, buspirone)	Monitor clinically; may require a dose increase or use of an alternate psychotropic drug.

Abbreviations: CCR5, C chemokine receptor type 5; CYP, cytochrome P450; FDA, US Food and Drug Administration; HIV, human immunodeficiency virus; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; RFB, rifabutin; RIF, rifampin; RPT, rifapentine; TDF, tenofovir disoproxil fumarate; TDM, therapeutic drug monitoring; TSH, thyroid-stimulating hormone.

[a] See the following useful websites for updated information regarding drug interactions: AIDSinfo, Centers for Disease Control and Prevention, University of California San Francisco, University of Liverpool, Indiana University, and University of Maryland.

Dosing Recommendations for Adult Patients with Reduced Renal Function[a]

Drug	Change in Frequency?	Recommended Dose and Frequency for Patients With Creatinine Clearance <30 mL/min, or Patients Receiving Hemodialysis
Isoniazid	No	300 mg once daily, or 900 mg 3 times/wk
Rifampin	No	600 mg once daily, or 600 mg 3 times/wk
Pyrazinamide	Yes	25–35 mg/kg/dose 3 times/wk (not daily)
Ethambutol	Yes	20–25 mg/kg/dose 3 times/wk (not daily)
Levofloxacin	Yes	750–1000 mg/dose 3 times/wk (not daily)
Moxifloxacin	No	400 mg once daily
Cycloserine	Yes	250 mg once daily, or 500 mg/dose 3 times/wk[b]
Ethionamide	No	250–500 mg/dose daily
Para-amino salicylic acid	No	4 g/dose twice daily
Streptomycin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)
Capreomycin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)
Kanamycin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)
Amikacin	Yes	15 mg/kg/dose 2-3 times/wk (not daily)

- Standard doses are given unless there is intolerance.
- The medications should be given after hemodialysis on the day of hemodialysis.
- Monitoring of serum drug concentrations should be considered to ensure adequate drug absorption, without excessive accumulation, and to assist in avoiding toxicity.
- Data currently are not available for patients receiving peritoneal dialysis. Until data become available, begin with doses recommended for patients receiving hemodialysis and verify adequacy of dosing using serum concentration monitoring.
- In patients with 30–50 mL/min creatinine clearance, standard doses are used by experts, but measurement of serum concentrations 2 and 6 hours after timed administration can be used to assist with optimizing drug dosages.

[a] Including adult patients receiving hemodialysis.

[b] The appropriateness of 250-mg daily doses has not been established. There should be careful monitoring for evidence of neurotoxicity.

POTENTIAL REGIMENS FOR THE MANAGEMENT OF PATIENTS WITH DRUG-RESISTANT PULMONARY TUBERCULOSIS WHEN 2003 TREATMENT GUIDELINES ARE USED

MMWR, June 20, 2003, p. 69

Pattern of drug resistance	Suggested regimen	Duration of treatment (mo)	Comments
INH (± SM)	RIF, PZA, EMB (an FQN may strengthen the regimen for patients with extensive disease)	6	In BMRC trials, 6-mo regimens have yielded ≥95% success rates despite resistance to INH if four drugs were used in the initial phase and RIF plus EMB or SM was used throughout.* Additional studies suggested that results were best if PZA was also used throughout the 6 mo (Rating BII).† Fluoroquinolones were not employed in BMRC studies, but may strengthen the regimen for patients with more extensive disease (Rating BIII). INH should be stopped in cases of INH resistance (see text for additional discussion).
INH and RIF (± SM)	FQN, PZA, EMB, IA, ± alternative agent	18–24	In such cases, extended treatment is needed to lessen the risk of relapse. In cases with extensive disease, the use of an additional agent (alternative agents) may be prudent to lessen the risk of failure and additional acquired drug resistance. Resectional surgery may be appropriate (see text).
INH, RIF (± SM), and EMB or PZA	FQN (EMB or PZA if active), IA, and two alternative agents	24	Use the first-line agents to which there is susceptibility. Add two or more alternative agents in case of extensive disease. Surgery should be considered (see text).
RIF	INH, EMB, FQN, supplemented with PZA for the first 2 months (an IA may be included for the first 2–3 months for patients with extensive disease)	12–18	Daily and three times weekly regimens of INH, PZA, and SM given for 9 mo were effective in a BMRC trial‡ (Rating BI). However, extended use of an injectable agent may not be feasible. It is not known if EMB would be as effective as SM in these regimens. An all-oral regimen for 12–18 mo should be effective (Rating BIII). But for more extensive disease and/or to shorten duration (e.g., to 12 months), an injectable agent may be added in the initial 2 mo of therapy (Rating BIII).

Definition of abbreviations: BMRC = British Medical Research Council; EMB = ethambutol; FQN = fluoroquinolone; IA = injectable agent; INH = isoniazid; PZA = pyrazinamide; RIF = rifampin; SM = streptomycin.

FQN = Fluoroquinolone; most experience involves ofloxacin, levofloxacin, or ciprofloxacin.

IA = Injectable agent; may include aminoglycosides (streptomycin, amikacin, or kanamycin) or the polypeptide capreomycin.

Alternative agents = Ethionamide, cycloserine, *p*-aminosalicylic acid, clarithromycin, amoxicillin-clavulanate, linezolid.

* Source: Mitchison DA, Nunn AJ. Influence of initial drug resistance on the response to short-course chemotherapy of pulmonary tuberculosis. Am Rev Respir Dis 1986;133:423–430.

† Source: Hong Kong Chest Service, British Medical Research Council. Five-year follow-up of a controlled trial of five 6 month regimens of chemotherapy for tuberculosis. Am Rev Respir Dis 1987;136:1339–1342.

‡ Source: Hong Kong Chest Service, British Medical Research Council. Controlled trial of 6-month and 9-month regimens of daily and intermittent streptomycin plus isoniazid plus pyrazinamide for pulmonary tuberculosis in Hong Kong. Am Rev Respir Dis 1977;115:727–735.

Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003;52(No. RR-11): 69.

TB TREATMENT IN SPECIAL SITUATIONS

Treating Culture-Negative Pulmonary TB

Preferred Regimen: **RIF/INH/PZA/EMB (RIPE)**	Initial Phase: RIPE x 2 months 40 (M-F) doses	Continuation Phase: RIPE x 2 months 40 (M-F) doses
Alternate Regimen: **RIF/INH/PZA/EMB (RIPE)**	Initial Phase: RIPE x 2 months 40 (M-F) doses	Continuation Phase: RIF and INH x 2 months 40 (M-F) doses

CONSULT TB EXPERTS AT SNTC (800-4TB-INFO) about treatment recommendations for drug-resistant tuberculosis**.**

BOX 3. Criteria for determining when, during therapy, a patient with pulmonary tuberculosis (TB) has become noninfectious*

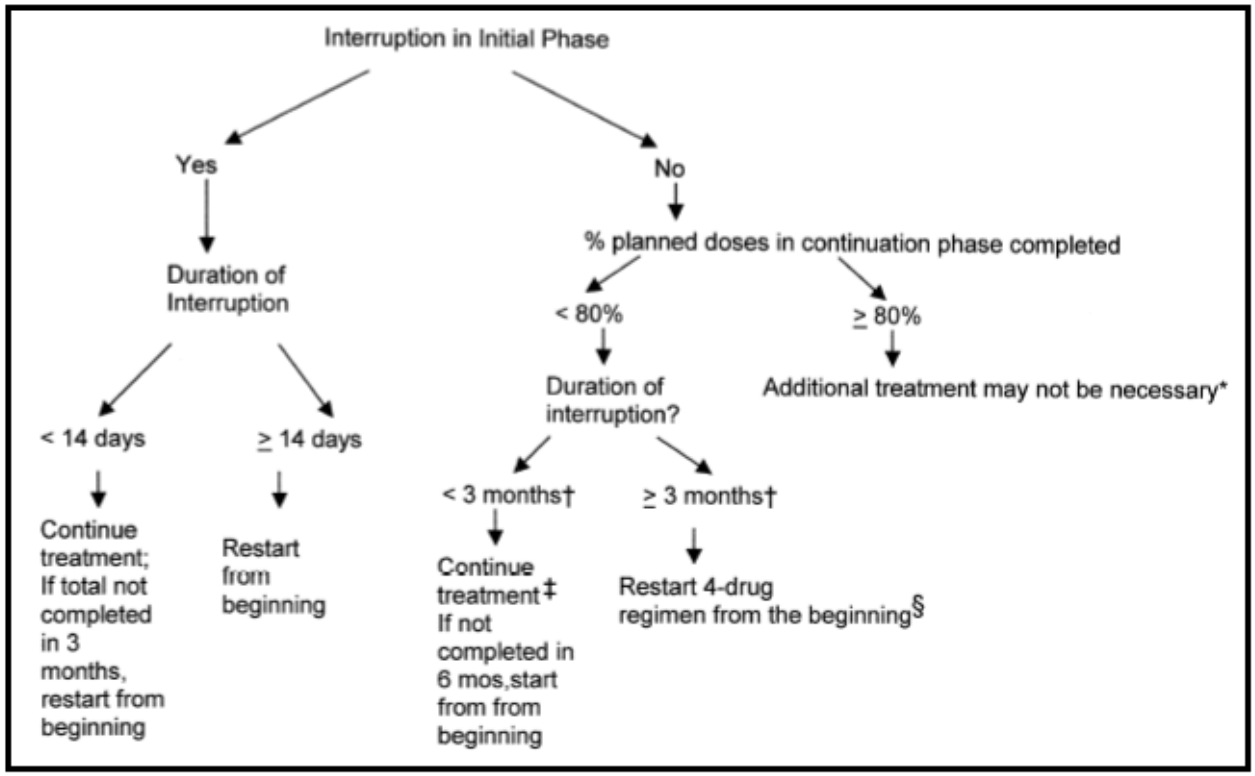
- **Patient has negligible likelihood of multidrug-resistant TB (no known exposure to multidrug-resistant tuberculosis and no history of prior episodes of TB with poor compliant during treatment).**
- **Patient has received standard multidrug anti-TB therapy for 2–3 weeks. (For patients with sputum acid-fast bacilli [AFB] smear results that are negative or rarely positive, threshold for treatment is 5–7 days.)**
- **Patient has demonstrated complete adherence to treatment (e.g., is receiving directly observed therapy).**
- **Patient has demonstrated evidence of clinical improvement (e.g., reduction in the frequency of cough or reduction of the grade of the sputum AFB smear result).**
- **All close contacts of patients have been identified, evaluated, advised, and, if indicated, started on treatment for latent TB infection. This criterion is critical, especially for children aged <4 years and persons of any age with immunocompromising health conditions (e.g., HIV infection).**
- **While in hospital for any reason, patients with pulmonary TB should remain in airborne infection isolation until they 1) are receiving standard multidrug anti-TB therapy; 2) have demonstrated clinical improvement; and 3) have had three consecutive AFB-negative smear results of sputum specimens collected 8–24 hours apart, with at least one being an early morning specimen. Hospitalized patients returning to a congregate setting (e.g., a homeless shelter or detention facility) should have three consecutive AFB-negative smear results of sputum specimens collected >8 hours apart before being considered noninfectious.**

Source: http://www.cdc.gov/MMWR/PDF/rr/rr5412.pdf (Box 3, p 9)

* These criteria for absence of infectivity with treatment should be considered general guidelines. Decisions about infectivity of a person on treatment for TB should depend on the extent of illness and the specific nature and circumstances of the contact between the patient and exposed persons.

MANAGEMENT OF TREATMENT INTERRUPTIONS

MMWR, June 20, 2003 41



* Patients who were initially AFB smear-positive should receive additional therapy.
† Recheck smears and cultures (if positive, check drug susceptibility results). Start DOT if not already being used.
‡ If repeat culture is positive, restart four-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, continue therapy to complete regimen within 9 months of original start date.
§ If repeat culture is positive, continue four-drug regimen while waiting for drug susceptibility results. If repeat culture is negative, consider stopping therapy if patient has received a total of 9 months of therapy.

Centers for Disease Control and Prevention. Treatment of Tuberculosis, American Thoracic Society, CDC, and Infectious Diseases Society of America. MMWR 2003;52(No. RR-11): 5.

II. MANAGEMENT OF TB INFECTION

BOX 1. Risk factors for *Mycobacterium tuberculosis* infection

Persons at increased risk* for *M. tuberculosis* infection

- close contacts of persons known or suspected to have active tuberculosis;
- foreign-born persons from areas that have a high incidence of active tuberculosis (e.g., Africa, Asia, Eastern Europe, Latin America, and Russia);
- persons who visit areas with a high prevalence of active tuberculosis, especially if visits are frequent or prolonged;
- residents and employees of congregate settings whose clients are at increased risk for active tuberculosis (e.g., correctional facilities, long-term care facilities, and homeless shelters);
- health-care workers who serve clients who are at increased risk for active tuberculosis [disease];
- populations defined locally as having an increased incidence of latent *M. tuberculosis* infection or active tuberculosis, possibly including medically underserved, low-income populations, or persons who abuse drugs or alcohol; and
- infants, children, and adolescents exposed to adults who are at increased risk for latent *M. tuberculosis* infection or active tuberculosis.

Source: Based on CDC. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6).

* Persons with these characteristics have an increased risk for *M. tuberculosis* infection compared with persons without these characteristics.

DIRECTLY OBSERVED PREVENTIVE THERAPY (DOPT) FOR LATENT TB INFECTION

A major step in controlling TB in a community is to make sure that a patient who is being treated for latent TB infection (LTBI) completes a course of treatment. DOPT is the only way to ensure that these patients are adherent to the medication. As Kentucky is experiencing a decline in the number of TB cases, it is time to put a stronger focus on treating latent TB infection.

The Kentucky TB Control Program is advocating that the LHDs provide DOPT to higher risk patients, as well as to children. Children can be the most difficult clients when it comes to taking their medication. By providing DOPT, the health department not only prevents future cases of TB, but also provides a valuable service to families.

Members of the groups below are considered high-risk individuals when it comes to being adherent to taking their medications. If found to have latent TB infection, members of these groups must be placed on DOPT:

- Children and adolescents
- Contacts to a case with active TB disease
- Homeless individuals
- Persons who abuse substances
- Persons with a history of treatment non-adherence
- Immunocompromised patients, especially HIV-infected

MEDICATIONS TO TREAT LATENT TUBERCULOSIS INFECTION: DOSES, TOXICITIES, AND MONITORING REQUIREMENTS

MMWR, June 9, 2000, pp. 28, 29

	Oral dose (mg/kg) (maximum dose)						
	Daily		Twice weekly*				
Drug	Adults	Children	Adults	Children	Adverse reactions	Monitoring	Comments
Isoniazid	5 (300 mg)	10–20 (300 mg)	15 (900 mg)	20–40 (900 mg)	Rash Hepatic enzyme elevation Hepatitis Peripheral neuropathy Mild central nervous system effects Drug interactions resulting in increased phenytoin (Dilantin) or Disulfiram (Antabuse) levels	Clinical monitoring monthly Liver function tests† at baseline in selected cases‡ and repeat measurements if: Baseline results are abnormal Patient is pregnant, in the immediate postpartum period, or at high risk for adverse reactions Patient has symptoms of adverse reactions	Hepatitis risk increases with age and alcohol consumption Pyridoxine (vitamin B6, 10–25 mg/d) might prevent peripheral neurophathy and central nervous system effects
Rifampin	10 (600 mg)	10–20 (600 mg)	10 (600 mg)	—	Rash Hepatitis Fever Thrombocytopenia Flu-like symptoms Orange-colored body fluids (secretions, urine, tears)	Clinical monitoring at weeks 2, 4, and 8 when pyrazinamide given Complete blood count, platelets, and liver function tests† at baseline in selected cases‡ and repeat measurements if Baseline results are abnormal Patient has symptoms of adverse reactions	Rifampin is contraindicated or should be used with caution in human immunodeficiency virus (HIV)-infected patients taking protease inhibitors (PIs) or nonnucleoside reverse transcriptase inhibitors (NNRTIs) Decreases levels of many drugs (e.g., methadone, coumadin derivatives, glucocorticoids, hormonal contraceptives, estrogens, oral hypoglycemic agents, digitalis, anticonvulsants, dapsone, ketoconazole, and cyclosporin) Might permanently discolor soft contact lenses
Rifabutin	5 (300 mg)§	—	5 (300 mg)§	—	Rash Hepatitis Fever Thrombocytopenia Orange-colored body fluids (secretions, urine, tears) With increased levels of rifabutin Severe arthralgias Uveitis Leukopenia	Clinical monitoring at Weeks 2, 4, and 8 when pyrazinamide given Complete blood count, platelets, and liver function tests† at baseline in selected cases‡ and repeat measurements if Baseline results are abnormal Patient has symptoms of adverse reactions Use adjusted daily dose of rifabutin and monitor for decreased antiretroviral activity and for rifabutin toxicity if rifabutin taken concurrently with PIs or NNRTIs§	Rifabutin is contraindicated for HIV-infected patients taking hard-gel saquinavir or delavirdine; caution is also advised if rifabutin is administered with soft-gel saquinavir Reduces levels of many drugs (e.g., PIs, NNTRIs, methadone, dapsone, ketoconazole, coumadin derivatives, hormonal contraceptive, digitalis, sulfonylureas, diazepam, ß-blockers, anticonvulsants, and theophylline) Might permanently discolor contact lenses
Pyrazinamide	15–20 (2.0 g)		50 (4.0 g)	—	Gastrointestinal upset Hepatitis Rash Arthralgias Gout (rare)	Clinical monitoring at Weeks 2, 4, and 8 Liver function tests† at baseline in selected cases‡ and repeat measurements if Baseline results are abnormal Patient has symptoms of adverse reactions	Treat hyperuricemia only if patient has symptoms Might make glucose control more difficult in persons with diabetes Should be avoided in pregnancy but can be given after first trimester

*All intermittent dosing should be administered by directly observed therapy.
† AST or ALT and serum bilirubin.
‡ HIV infection, history of liver disease, alcoholism, and pregnancy.
§ If nelfinavir, indinavir, amprenavir, or ritonavir is administered with rifabutin, blood concentrations of these protease inhibitors decrease. Thus, the dose of rifabutin is reduced from 300 mg to 150 mg/d when efavirenz is administered with rifabutin, blood concentrations of rifabutin decrease. Thus, when rifabutin is used concurrently with efavirenz, the daily dose of rifabutin should be increased from 300 mg to 450 mg or 600 mg. Pharmacokinetic studies suggest that rifabutin might be given at usual doses with nevirapine. It is not currently known whether dose adjustment of rifabutin is required when used concurrently with soft-gel saquinavir. For patients receiving multiple PIs or a PI in combination with an NNRTI, drug interactions with rifabutin are likely more complex; in such situations, the use of rifabutin is not recommended until additional data are available.

QuantiFERON® Test

A blood test for latent tuberculosis infection (LTBI) has been recently licensed. The Kentucky Tuberculosis Control Program does not recommend this test for general use pending results of ongoing studies of the sensitivity and specificity of the test in various sub-populations. At this time, the Kentucky State Laboratory is not conducting the test.

QuantiFERON®-TB Gold In-Tube and T-SPOT®.*TB*

These two blood assays for *Mycobacterium tuberculosis* (BAMT) have been licensed by the FDA. The Kentucky Tuberculosis Program does not recommend either of these tests for general use pending results of ongoing studies of the sensitivity and specificity of these tests in various sub-populations. At this time, the Kentucky State Laboratory is not performing BAMT tests with either assay.

Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. MMWR 2000;49(No. RR-6):28-29.

Regimen Options for Treatment of Latent TB Infection in HIV-Negative Persons

Drug	Regimens				Comments
	Daily		Twice Weekly✞		
	Children	Adults	Children	Adults	
	Duration	Duration	Duration	Duration	
INH	9 months	9 months	9 months	9 months	Minimum of 180 (M-F) or 270 (M-Sun) doses administered within 12 months Twice-weekly regimens should consist of at least 76 doses administered within 12 months. Recommended regimen for pregnant women Contraindicated for persons who have active hepatitis and end-stage liver disease
INH and Rifapentine	_____	Once Weekly for 3 months	_____	-_____	Treatment for: • Persons 12 years or older • Must be given by directly observed preventive therapy Once weekly regimen should consist of at least 12 doses administered within 4 months. Not recommended for persons who are: • Younger than 2 years old • Living with HIV/AIDS taking antiretroviral treatment • Presumed infected with INH or RIF-resistant M. tuberculosis, and • Women who are pregnant or expect to become pregnant within the 12-week regimen.

Drug	Regimens				Comments
	Daily		Twice Weekly✞		
	Children	Adults	Children	Adults	
	Duration	Duration	Duration	Duration	
RIF	4 months	4 months	Not recommended		Minimum of 120 doses administered within 6 months For persons who are contacts of patients with INH-resistant, RIF-susceptible TB May be used for patients who cannot tolerate INH or PZA
WARNING: Fatal and Severe Liver Injuries Have Been Associated With Rifampin (RIF) and Pyrazinamide (PZA) Treatment for LTBI					
RIF and PZA	Not recommended	2 months	Not recommended	2 or 3 months	**CONSULT TB EXPERTS AT SNTC (800-4TB-INFO) BEFORE USING.** Contraindicated for persons who have active hepatitis and end-stage liver disease. Avoid PZA for pregnant women because of the risk of adverse effects to the fetus. Minimum of 60 doses to be administered within 3 months. Twice-weekly regimens should consist of at least 16 doses to be administered for 2 months or 24 doses to be administered for 3 months. May be used for INH-intolerant patients. This regimen has not been evaluated in HIV-negative persons.

INH – isoniazid, RIF – rifampin, RFB – rifabutin, PZA – pyrazinamide, EMB – ethambutol
✞ Directly observed treatment of LTBI should be used.
Centers for Disease Control and Prevention, Core Curriculum on Tuberculosis (2013)
Morbidity and Mortality, August 31, 2009, Vol. 50 / No. 34

Regimen Options for Treatment of Latent TB Infection for Persons with HIV Infection

<table>
<tr><th rowspan="3">Drug</th><th colspan="4">Regimens</th><th rowspan="3">Comments</th><th rowspan="3">Contraindications</th></tr>
<tr><th colspan="2">Daily</th><th colspan="2">Twice Weekly✞</th></tr>
<tr><th>Children
Duration</th><th>Adults
Duration</th><th>Children
Duration</th><th>Adults
Duration</th></tr>
<tr><td>INH</td><td>9 months</td><td>9 months</td><td>9 months</td><td>9 months</td><td>Minimum of 108 (M-F) or 270 (M-Sun) doses administered within 12 months

Twice-weekly regimens should consist of at least 76 doses administered within 12 months.

INH can be administered concurrently with NRTIs, PIs, or NNRTIs

Directly observed treatment of latent TB infection should be used when twice-weekly dosing is used</td><td>History of INH-induced reaction, including hepatic, skin or other allergic reactions, or neuropathy

Known exposure to person who has INH-resistant TB

Chronic severe liver disease</td></tr>
<tr><td>RIF
and
PZA*</td><td>Not recommended</td><td>2 months</td><td>Not recommended</td><td>2-3 months</td><td rowspan="2">Minimum of 60 doses to be administered within 3 months

Twice-weekly regimens should consist of at least 16 doses to be administered for 2 months or 24 doses to be administered for 3 months.

IF RFB is administered, patient should be monitored carefully for potential RFB drug toxicity and potential decreased antiretroviral drug activity.

Dose adjustments, alternative therapies, or other precautions might be needed when rifamycins are used (e.g., patient using hormonal contraceptives must be advised to use barrier methods, and patients using methadone require dose adjustments).

PIs or NNRTIs should generally not be administered concurrently with RIF; in this situation, an alternative is the use of RFB✞ and PZA.</td><td rowspan="2">History of a rifamycin-induced reaction, including hepatic, skin or other allergic reaction, or thrombocytopenia

Pregnancy

Chronic severe hyperuricemia

Chronic severe liver disease</td></tr>
<tr><td>RFB
and
PZA*</td><td>Not recommended</td><td>2 months</td><td>Not recommended</td><td>2-3 months</td></tr>
</table>

WARNING: Fatal and Severe Liver Injuries Have Been Associated With Rifampin (RIF) and Pyrazinamide (PZA) Treatment for LTBI

INH – isoniazid; PZA- pyrazinamide; RFB- rifabutin; RIF- rifampin; DOPT- directly observed preventive therapy; PIs – protease inhibitors; NNRTIs – nonnucleoside reverse transcriptase inhibitors; NRTIs – nucleoside reverse transcriptase inhibitors

*For patients with intolerance to PZA, some experts recommend the use of a rifamycin (RIF or RFB) alone for preventive treatment. Most experts agree that available data support the recommendation that this treatment can be administered for a short a duration as 4 months, although some experts would treat for 6 months.

PLANNING A CONTACT INVESTIGATION

Confirmed TB Cases:
A contact investigation is required for all confirmed cases that have infectious forms of TB disease (e.g., TB disease of the lungs, airways, or larynx).

Suspected TB Cases: For suspect cases with AFB-negative sputum smears or sputum smears not performed, the contact investigation process should be started if the case has abnormal chest x-ray findings consistent with TB disease.

For suspect cases with AFB-negative sputum smear results and no pulmonary cavities, a contact investigation should only be considered for certain circumstances, such as if the suspect was identified during an outbreak or source case investigation that included vulnerable or susceptible contacts.

Extrapulmonary TB Disease:
Persons with extrapulmonary TB disease are usually noninfectious unless they also have pulmonary TB disease, TB disease located in the oral cavity or the larynx, or extrapulmonary disease that includes an open abscess or lesion in which the concentration of organisms is high **Pulmonary TB should always be ruled out when there is a diagnosis of extrapulmonary disease.**

Initiating a Contact Investigation:
The contact investigation process should be started for persons suspected of having infectious TB disease, even before confirmation (See "Initial Assessment of Contacts" in this section).Contact Investigations of persons with acid-fast bacilli (AFB)-positive sputum smears, and cavitary TB are assigned the highest priority. However, even if these conditions are not present, contact investigations should be considered if a chest radiograph is consistent with pulmonary TB. A positive result from an approved nucleic acid amplification (NAA) test supports a decision to initiate an investigation. **Because waiting for a sputum or respiratory culture result delays initiation of contact investigations, delay should be avoided if any contacts are especially vulnerable or susceptible to TB disease.** If it is later determined that the suspect case does not have infectious TB disease, the contact investigation should be stopped.

The Goals of a Contact Investigation:
The goals of a contact investigation are 1) rapid identification of individuals who are high priority contacts to a known or suspected case of pulmonary, laryngeal, or pleural TB; 2) timely initiation of appropriate treatment for those persons determined to be recently infected or exposed with a significant risk for progression to disease; and 3) identification and treatment of additional individuals found to have suspected TB disease in order to prevent further spread of disease.

Consult the State TB Program if you are planning a contact investigation for more than 10 people (e.g. a school, college, or large company). For complete guidelines on structuring a contact investigation see the "Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis," MMWR 2005:54 (No. RR-14).

Determining the Infectious Period for a Patient with Active TB Disease

Determining the infectious period for a case with active TB disease focuses the investigation on those contacts most likely to be at risk for infection and sets the timeframe for testing contacts. Because the start of the infectious period cannot be determined with precision by available methods, a practical estimation is necessary. Per CDC guidelines, an assigned start date, that is **3 months before** symptom onset or first positive finding consistent with active TB disease, is recommended (Table, p. 50). In certain circumstances, an even earlier start date should be used. For example, a patient (or the patient's associates) might have been aware of protracted illness (in extreme cases, >1 year). Information from the patient interview and from other sources should be assembled to assist in estimating the infectious period. Helpful details are the approximate dates that TB symptoms were noticed, mycobacteriologic results, and extent of disease (especially the presence of large lung cavities, which imply prolonged illness and infectiousness).

The infectious period is closed when the following criteria are satisfied: 1) effective treatment (as demonstrated by *M. tuberculosis* susceptibility results) for ≥2 weeks; 2) diminished symptoms; and 3) mycobacteriologic response (e.g., decrease in grade of sputum smear positivity detected on sputum-smear microscopy). The exposure period for individual contacts is determined by how much time they spent with the index patient during the infectious period. Multidrug-resistant TB (MDR TB) can extend infectiousness if the treatment regimen is ineffective. Any index patient with signs of extended infectiousness should be continually reassessed for recent contacts.

Criteria that are more stringent should be applied for setting the end of the infectious period if particularly susceptible contacts are involved. A patient returning to a congregate living setting or to any setting in which susceptible persons might be exposed should have at least three consecutive negative sputum AFB smear results from sputum collected ≥8 hours apart (with one specimen collected during the early morning) before being considered noninfectious.

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 12.

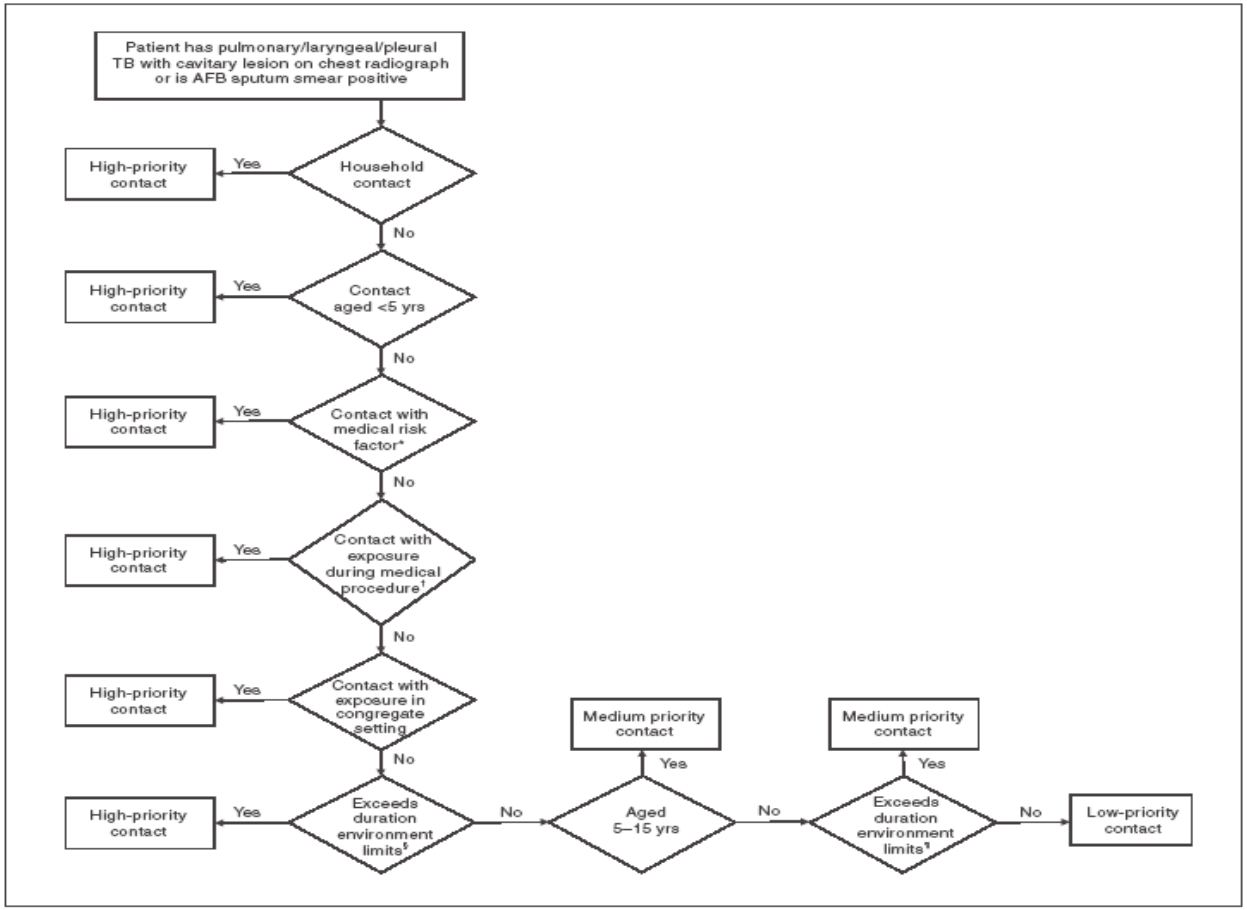
Initial Assessment of Contacts

During the initial contact encounter, which should be accomplished within **3 working days** of the contact having been listed in the investigation, the investigator gathers background health information and makes a face-to-face assessment of the person's health. Performing a TB Risk Assessment and administering a TST or drawing blood for a BAMT at this time accelerates the diagnostic evaluation.

The health department record should include:

- Previous *M. tuberculosis* infection or active TB disease and related treatment;
- Contact's verbal report and documentation of previous TST or BAMT results;
- Current symptoms of active TB disease (e.g., cough, chest pain, hemoptysis, fever, chills, night sweats, appetite loss, weight loss, malaise, or easy fatigability);
- Medical conditions or risk factors making active TB disease more likely
    - HIV infection
    - Infants and children aged less than five years;
    - Persons who are receiving immunosuppressive therapy such as tumor necrosis factor--alpha (TNF-α) antagonists, systemic corticosteroids equivalent to ≥15 mg of prednisone per day, or immune suppressive drug therapy following organ transplantation;
    - Persons recently infected with *Mycobacterium tuberculosis* (within the past two (2) years;
    - Persons with a history of inadequately treated active TB disease;
    - Persons with silicosis, diabetes mellitus, chronic renal failure, leukemia, lymphoma, cancer of the head, neck, or lung;
    - Persons who have had a gastrectomy, or jejunoileal bypass;
    - Persons with low body weight (BMI < 19);
    - Cigarette smokers and persons who abuse drugs or alcohol.
- Mental health disorders (e.g., psychiatric illnesses and substance abuse disorders)
- Type, duration, and intensity of TB exposure; and
- Sociodemographic factors (e.g., age, race or ethnicity, residence, and country of birth) (see Data Management and Evaluation of Contact Investigations).

Prioritization of Contacts Exposed to Persons with Acid-Fast Bacilli (AFB) Sputum Smear-Positive or Cavitary Tuberculosis (TB) Cases



* Human immunodeficiency virus or other medical risk factor.
† Bronchoscopy, sputum induction, or autopsy.
§ Exposure exceeds duration/environment limits per unit time established by the health department for high-priority contacts.
¶ Exposure exceeds duration/environment limits per unit time established by the health department for medium-priority contacts.

Window-Period Prophylaxis

Primary prophylaxis of high-risk contacts:

Tuberculin skin test results might take 2-10 weeks to become positive after infection with *M. tuberculosis.* Thus, a contact's initial TST or BAMT result might be negative even if the person is infected. A second TST or BAMT should be performed 8-10 weeks after the contact's last exposure to the infectious patient, so the possibility of LTBI for those persons can be better evaluated. During the 8-10 week window period between a first and second skin test or BAMT, the following contacts with initially negative tuberculin skin test results or negative BAMT results should receive treatment for LTBI after active TB disease has been ruled out by clinical examination and chest radiograph:

- Contacts aged <5 years (with highest priority given to those aged <3 years) and
- Contacts with HIV infection or who are otherwise immunocompromised.

If the second TST result is negative (i.e. <5 mm) or the second BAMT is negative, the contact is immunocompetent (including immunocompetent young children) and no longer exposed to an infectious TB case, treatment for LTBI during the window period may be discontinued, and further follow-up is unnecessary.

If the second TST or BAMT result is negative but the contact is immunocompromised (e.g., with HIV infection), and an evaluation for active TB disease is negative, a full course of treatment for LTBI still should be completed.

If the second TST or BAMT result is negative but the person remains in close contact with an infectious TB case, treatment for LTBI should be continued if the contact is:

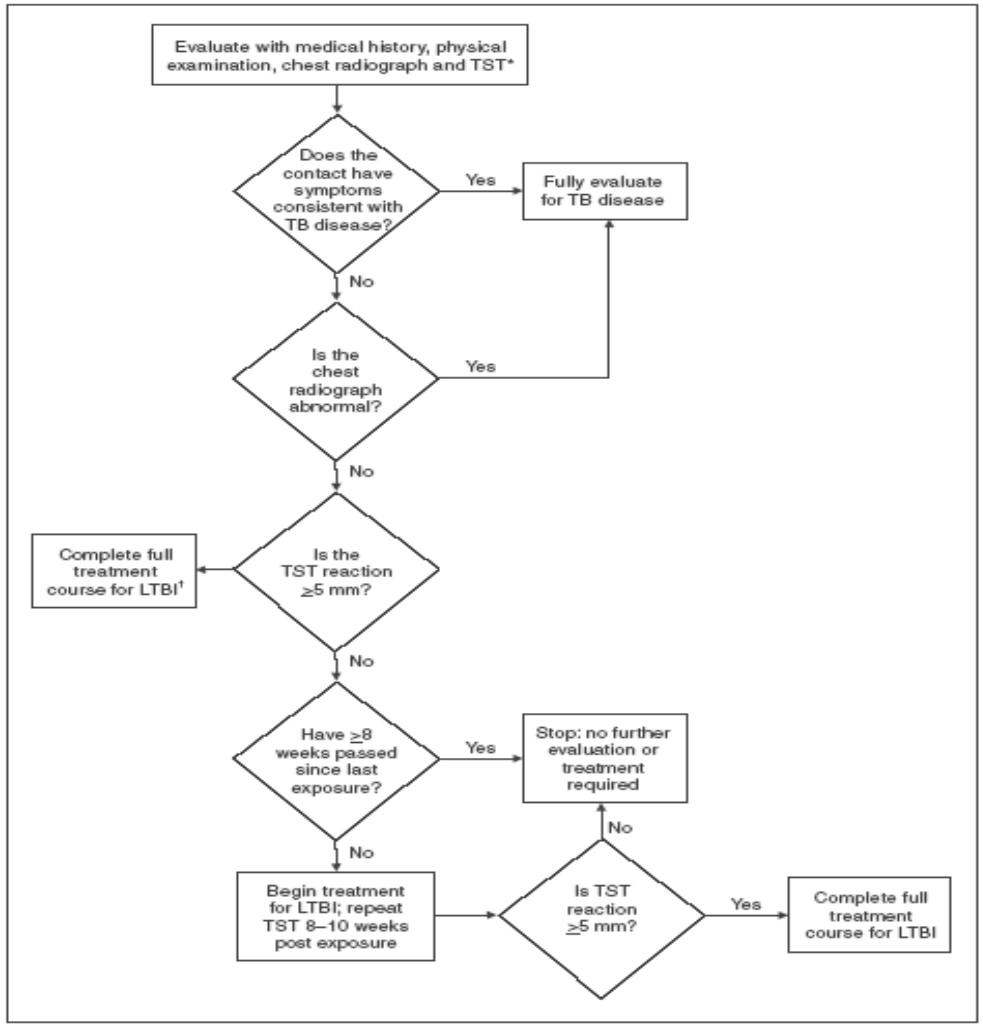
- Aged <5 years;
- Aged 5 through 15 years, at the clinician's discretion; or
- HIV-infected or otherwise immunocompromised.

The decision to treat individual contacts that have negative skin tests or negative BAMTs should take into consideration two factors:

- The frequency, duration, and intensity of exposure (even brief exposure to a highly infectious TB patient in a confined space probably warrants the same concern as extended exposure to less infectious TB cases); and
- Corroborative evidence of transmission from the index patient (e.g. a substantial fraction of contacts having TST or BAMT results classified as “positive” implies infectiousness).

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 15.

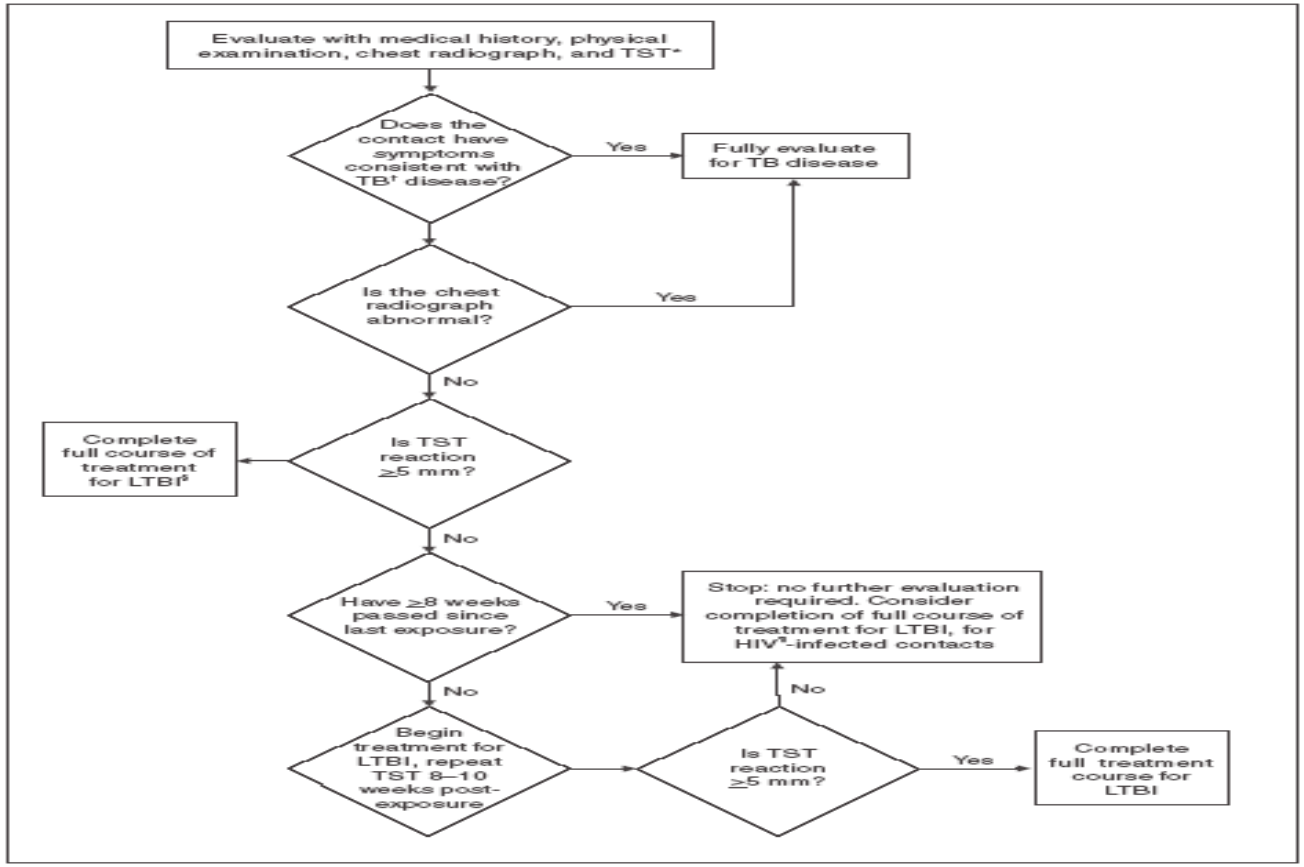
Evaluation, Treatment, and Follow-Up of Tuberculosis (TB) Contacts Aged < 5 Years



* Tuberculin skin test.
† Latent TB infection.

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 15.

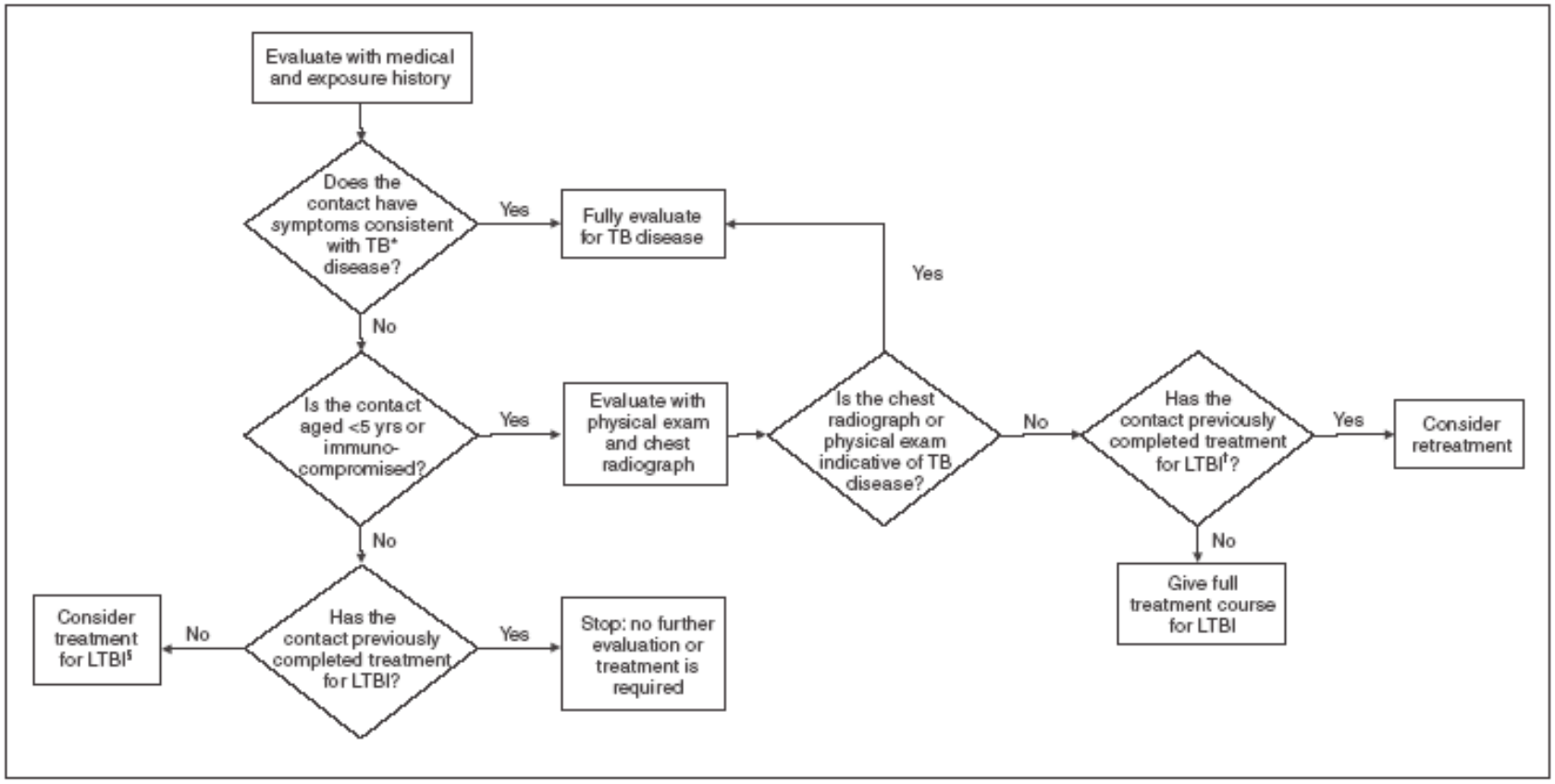
Evaluation, Treatment, and Follow-Up of Immunocompromised Contacts



* Tuberculin skin test.
† Tuberculosis.
§ Latent TB infection.
¶ Human immunodeficiency virus.

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 16.

Evaluation, Treatment, and Follow-Up of Contacts with a Documented Previously Positive Tuberculin Skin Test



* Tuberculosis.
† Latent TB infection.
§ Before initiation of treatment, contacts should be evaluated fully for TB disease.

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 19.

Time Frames for Initial Follow-up of Contacts of Persons Exposed to Tuberculosis (TB)

Type of contact	Business days from listing of a contact to initial encounter*	Business days from initial encounter to completion of medical evaluation†
High-priority contact: index case AFB§ sputum smear positive or cavitary disease on chest radiograph (see Figure 2)	7	5
High-priority contact: index case AFB sputum smear negative (see Figure 3)	7	10
Medium-priority contact: regardless of AFB sputum smear or culture result (see Figures 2–4)	14	10

SOURCE: California Department of Health Services Tuberculosis Control Branch; California Tuberculosis Controllers Association. Contact investigation guidelines. Berkeley, CA: California Department of Health Services; 1998.

* A face-to-face meeting that allows the public-health worker to assess the overall health of the contact, administer a tuberculin skin test, and schedule further evaluation.

† The medical evaluation is complete when the contact's status with respect to *Mycobacterium tuberculosis* infection or TB disease has been determined. A normal exception to this schedule is the delay in waiting for final mycobacteriologic results, but this applies to relatively few contacts.

§ Acid-fast bacilli.

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 9.

Guidelines for Estimating the Beginning of the Period of Infectiousness of Persons with Tuberculosis (TB), by Index Case Characteristic

Characteristic			
TB symptoms	AFB* sputum smear positive	Cavitary chest radiograph	Recommended minimum beginning of likely period of infectiousness
Yes	No	No	3 months before symptom onset or first positive finding (e.g., abnormal chest radiograph) consistent with TB disease, whichever is longer
Yes	Yes	Yes	3 months before symptom onset or first positive finding consistent with TB disease, whichever is longer
No	No	No	4 weeks before date of suspected diagnosis
No	Yes	Yes	3 months before first positive finding consistent with TB

SOURCE: California Department of Health Services Tuberculosis Control Branch; California Tuberculosis Controllers Association. Contact investigation guidelines. Berkeley, CA: California Department of Health Services; 1998.
* Acid-fast bacilli.

MMWR Guidelines for the Investigation of Contacts of Persons with Infectious Tuberculosis, Recommendations from the National Tuberculosis Controllers Association and CDC, December 16, 2005, Vol. 54, No. RR-15, p 7.

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World Health Organization Global TB Database Estimated Incidence

This information is listed in the forms and teaching sheets listing of the CCSG at http://chfs.ky.gov/dph/Local+Health+Department.htm.